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NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* J. W. LOWN

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STUDIES IN PSEUDOHALOGEN CHEMISTRY

by

ALUMMOOTTIL V. JOSHUA ©

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled Studies in Pseudohalogen Chemistry

submitted by Alummoottil V. Joshua

in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

J W Lown
Supervisor

H J Liu

R K Brown

Daniel Swern
External Examiner

Date Oct 8 '75

To my Friends and Relatives.

ABSTRACT

Iodonium nitrate in chloroform-pyridine at room temperature undergoes a *trans* stereospecific electrophilic addition to alkenes to form (i) iodoalkyl nitrates, (ii) iodoalkyl pyridinium nitrates, and/or (iii) alkenyl pyridinium iodides depending on the substrate. The addition is sensitive to steric hindrance effects and anti-Markovnikov addition is commonly encountered. In similar additions to conjugated dienes 1,2-additions in a Markovnikov fashion to form 1:1 adducts of the type (ii) are the rule. Iodonium nitrate is unreactive towards α,β-unsaturated carbonyl compounds. Terminal acetylenes give alkynyl iodides in fair yield. Phenols and anilines afford aromatic substitution products.

With olefinic alcohols, iodonium nitrate in chloroform-pyridine gives (iv) hydroxyiodoalkyl nitrates, (v) hydroxyiodoalkyl pyridinium nitrates and/or (vi) five and six-membered cyclic ethers where this is structurally possible. Parallel reactions in chloroform-*sym*-collidine give three, four and five-membered cyclic ethers as well as products of the type (iv). The *trans* stereospecific addition of iodonium nitrate to cyclohex-2-en-1-ol indicates that the iodonium ion is formed *cis* to the hydroxy group. The stereochemical directing influence of hydroxy group in other cyclic systems has also been investigated. Examples of participation by neighboring carboxyl group and sulfur are provided. The iodonium nitrate-pyridine complex has been isolated as a crystalline solid and shown to undergo a stoichiometric and stereospecific addition to (*E*)-4,4-dimethylpent-2-ene.

The stereochemistry of the additions to alkenes was proven by relating the iodoalkyl nitrates to the corresponding epoxides for 4,4-dimethylpent-2-enes and by base catalyzed elimination of hydrogen iodide from the iodoalkyl pyridinium nitrates to the vinyl pyridinium iodides for but-2-enes. The addition to the less hindered (Z)-2-deuterostyrene is also stereospecific, eliminating the possibility of restricted rotation during addition.

The kinetic studies on the addition of iodonium nitrate were performed by following the disappearance of iodonium nitrate by a titration method. The reaction is shown to be of second order, first order in iodonium nitrate and first order in the olefin. Kinetic evidence for participation by hydroxy group is presented. The activation parameters for the addition of iodonium nitrate to a few olefins and olefinic alcohols have been determined.

The reactions of bromonium nitrate in chloroform-pyridine with unsaturated substrates were examined. Although it resembles iodonium nitrate in its reactions, certain differences are also found. These are explained in terms of the stability of the intermediate halonium ions.

Conjugated dienes, in addition to bromopyridinium salts, give 1,2-bromonitrates which rearrange to 1,4-bromonitrates. A concerted cyclic mechanism is postulated for the above rearrangement.

Although iodonium nitrate was unreactive towards 3,3,3-triphenylpropene, bromonium nitrate did react with it to give a pyridinium salt which arises as a result of phenyl migration. An example of participation by hydroxy group is also presented.

The stereochemistry of the additions was shown to be *trans* by performing additions to (*Z*) and (*E*) pairs of olefins and confirmed by addition to (*Z*)-2-deuterostyrene.

A series of iodoalkyl pyridinium nitrates and alkenyl pyridinium iodides were prepared and shown to possess significant anti-diabetic property.

ACKNOWLEDGEMENTS

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CHAPTER I

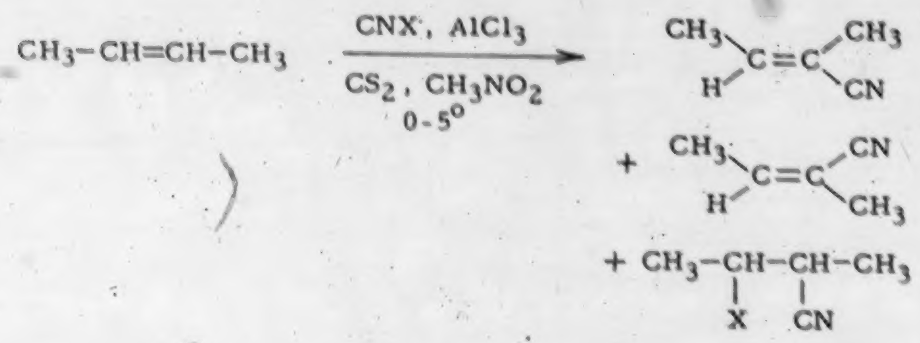
Introduction

The addition of pseudohalogens to unsaturated substrates has recently gained in importance through their synthetic and mechanistic investigations. These stereospecific reactions complement the methods for the stereospecific introduction of oxygen functions into the carbon skeleton, e.g. via opening of epoxides, hydroboration of olefins or reduction of ketones, by providing stereospecific routes for the introduction of other functional groups, particularly nitrogen functions into organic molecules. The growing importance of pseudohalogen addition is clearly revealed by the number of recent publications dealing with stereospecific routes for the synthesis of β-iodoazides[1], vinyl azides[2-5], azirines[6,7], aziridines[8-12], E-N-(2-iodoalkyl) carbamates[12], Z and E-2-aminoalcohols[12], oxazolidones[8], 1,2-diamines[13,14], aminosugars[15,16], azepines[17,18], 1-azetines[19,20], β-iodonitro, vinyl nitro, and nitroalkanes[21], chloroketones[22], N-cyanoimines and N-cyanoaziridines[23,24], N-cyanoazepines[25], episulfides[26] etc. These studies were also important from physical organic stand-point in providing additional evidence for the mechanism by which halogens, in general, add to unsaturated substrates. Much of the earlier work on the chemistry of pseudohalogens have been covered in review articles dealing with nitryl and nitrosyl halides[27], nitrosyl chloride[28], cyanogen[29], cyanogen bromide[30], and thiocyanogen[31]. Because of the enormous amount of information available on their chemistry, we will restrict our discussion mainly to halogen-containing pseudohalogens.

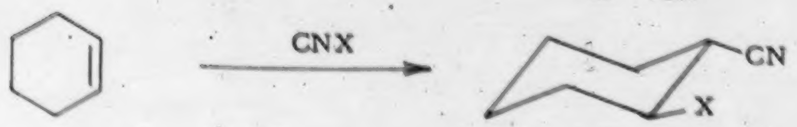
Pseudohalogens, in general, resemble halogens in their behaviour towards olefinic compounds. The reactivity and types of reactions undergone by different pseudohalogens vary to some extent, although certain similarities may also be seen.

Cyanogen halides

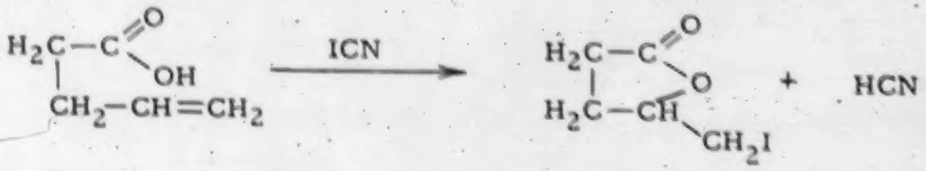
The cyanogen halides[32-34] can add to olefins at ambient temperatures, but require a Lewis acid catalyst. Substitution by nitrile group is a side reaction which predominates above 25° or in the absence of a catalyst at elevated temperatures. In the absence of the catalyst no reaction takes place between cyanogen halides and typical unsaturated compounds at ambient temperatures except between cyanogen iodide and γ,δ-unsautrated acids, the products being δ-iodopentanolactones, 1[35]. Under similar conditions cyanogen bromide



$CH_3-CH=CH-CH_3$
CNX, $AlCl_3$
CS_2, CH_3NO_2
0-5°
CH_3
CH_3
H
CN
+
CH_3
CN
H
CH_3
+ $CH_3-CH-CH-CH_3$
X
CN



X = Cl, Br, I

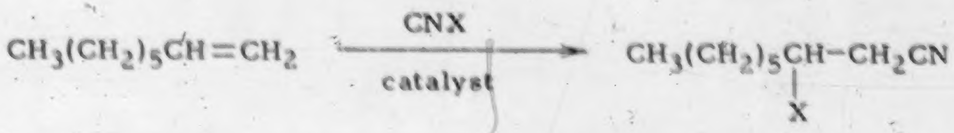


H_2C-C
O
OH
$CH_2-CH=CH_2$
ICN
H_2C-C
O
O
H_2C-CH
CH_2I
+
HCN

1

gave no reaction.

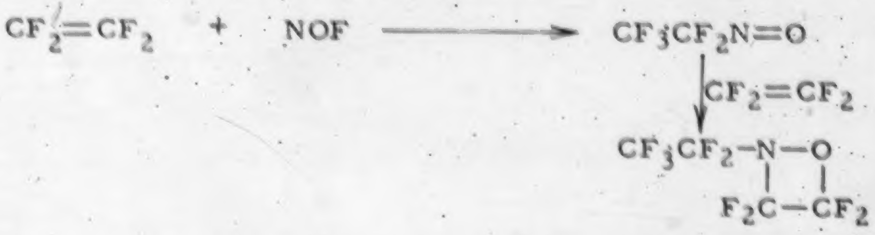
The reaction of cyanogen halides with unsaturated compounds proceeds by a free-radical mechanism, the CN radical being the initial attacking species. Cyanogen iodide is exceptional in its behaviour towards γ,δ-unsaturated acids, because of its greater polarizability and thus has sufficient electrophilic character to bring about lactonization. Cyanogen bromide, being less easily polarized, is unreactive towards such compounds.

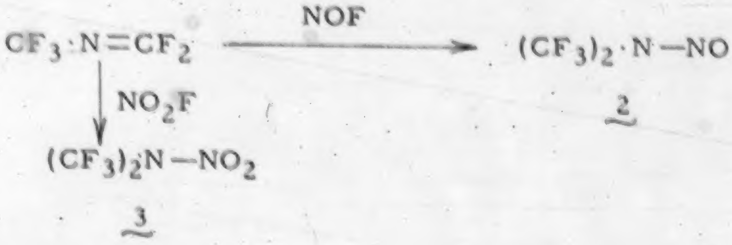


$$CH_3(CH_2)_5CH{=}CH_2 \xrightarrow[\text{catalyst}]{CNX} CH_3(CH_2)_5\underset{\displaystyle X}{\underset{|}{C}}H{-}CH_2CN$$

Nitrosyl and nitryl halides

Another interesting class of pseudohalogens, as far as reactivity and mechanism are concerned, is the nitrosyl and nitryl halides. Nitrosyl fluoride can be expected to be highly reactive and its reactions with fluoroolefins have been reported[36-38]. The addition of nitrosyl fluoride or nitryl fluoride to pentafluoroazapropene occurs rapidly and quantitatively at low temperatures to give N-nitroso[39] and N-nitrobis(trifluoromethyl)amine[40], 2 and 3, respectively.



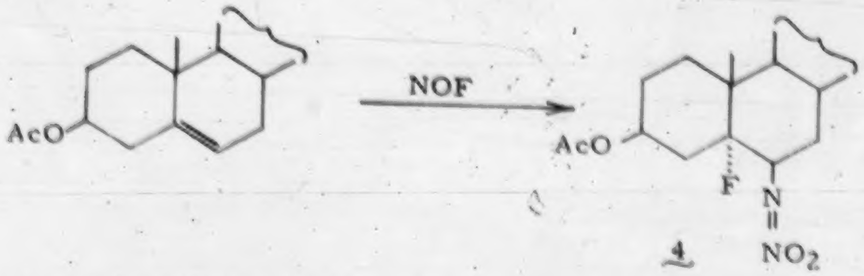


$$\begin{tikzcd} CF_3\cdot N{=}CF_2 \arrow[r, "NOF"] \arrow[d, "NO_2F"] & (CF_3)_2\cdot N{-}NO \\ (CF_3)_2N{-}NO_2 & \end{tikzcd}$$

2

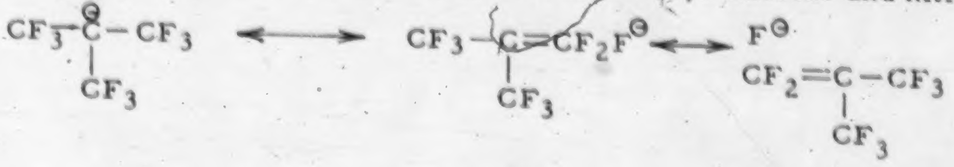
3

Reaction of nitrosyl fluoride with cholesteryl acetate provides the 5α-fluoro-6-(N-nitrosoimino) derivative[41], 4. This result is to be contrasted with the reaction of nitrosyl chloride with steroid-2-enes and 5-enes, which gave the corresponding chloronitrosteroids in good yield.



4

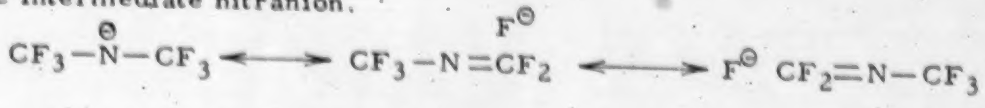
Both the direction of addition of nitrosyl fluoride and the qualitative order of reactivity of fluoroolefins [$(CF_3)_2\cdot C{=}CF_2 > CF_3\cdot CF{=}CF_2 > CF_2{=}CF_2$] indicate that initial attack is by the anionic portion of the adding reagent, the fluoride ion, to give a transition state with carbanionic character[38]. The direction of addition and order of reactivity are explicable in terms of greatest charge delocalization by "no-bond" resonance in a carbanion with the largest number of β-fluorine atoms. The carbanions can be stabilized by contribution from additional degenerate resonance extremes of the type, 5a and 5b. The ease of addition of nitrosyl fluoride and nitryl fluoride to pentafluoroazapropene is similarly explicable in terms of the intermediate nitranion.



$$CF_3-\overset{\ominus}{\underset{CF_3}{C}}-CF_3 \longleftrightarrow CF_3-\underset{CF_3}{C}{=}CF_2\,F^{\ominus} \longleftrightarrow F^{\ominus}\;CF_2{=}\underset{CF_3}{C}-CF_3$$

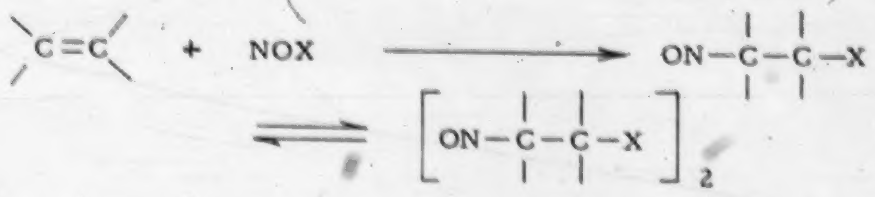
5a

5b



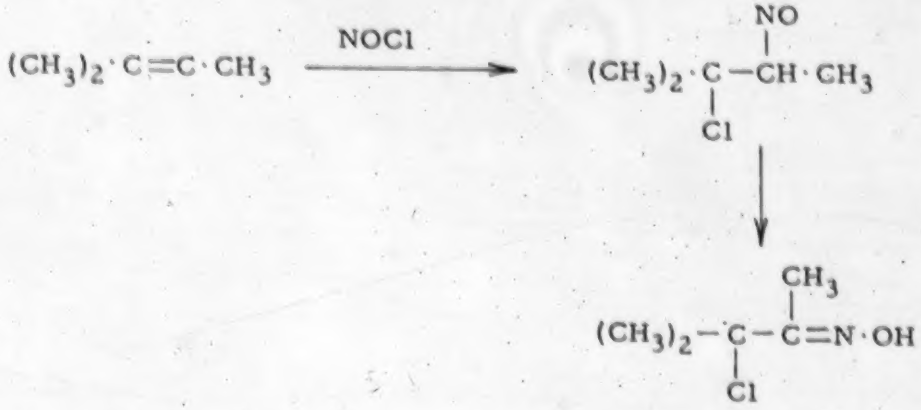
$$CF_3-\overset{\ominus}{N}-CF_3 \longleftrightarrow \overset{F^{\ominus}}{CF_3-N{=}CF_2} \longleftrightarrow F^{\ominus}\;CF_2{=}N-CF_3$$

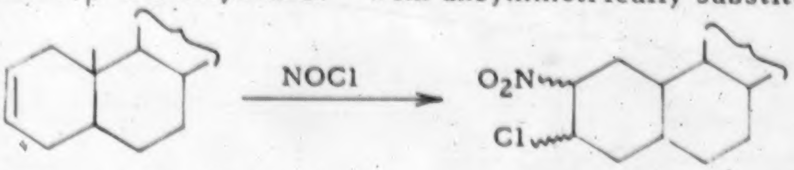
Nitrosyl chloride and nitrosyl bromide, which can be generated in situ, by the reaction between an alkyl nitrite and hydrochloric and hydrobromic acids respectively[44], readily undergo reaction with olefins to give nitrosohalides, which dimerise if unhindered[28].


C=C
+
NOX
ON—C—C—X
ON—C—C—X
2

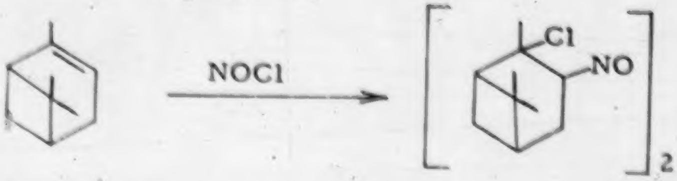
X = Cl, Br

The monomers can usually be recognized also, though these readily undergo prototropic change to give the oxime. In nitrosyl halide additions to olefins, the nitroso group is often oxidised by nitrosyl halide to the nitro- group[43]. Similar behaviour has been encountered[45] for the addition of nitrosyl chloride to phenylacetylenes, the products being α-chloro,β-nitrostyrenes. With unsymmetrically substituted olefins, addition of the nitroso- group to the less substituted carbon atom is generally observed as illustrated for the reaction between

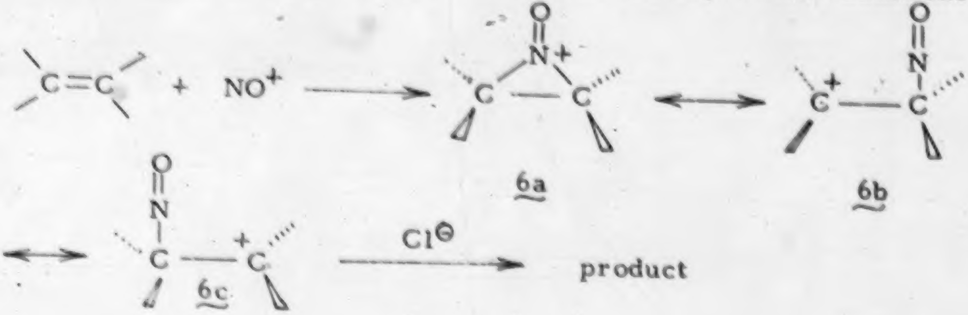

$(CH_3)_2\cdot C{=}C\cdot CH_3$
NOCl
NO
$(CH_3)_2\cdot C-CH\cdot CH_3$
Cl
CH_3
$(CH_3)_2-C-C{=}N\cdot OH$
Cl



nitrosyl chloride and ∝-pinene[46].



Based on the above considerations, a mechanism involving NO^+ and X^- has been generally assumed for nitrosyl halide additions.



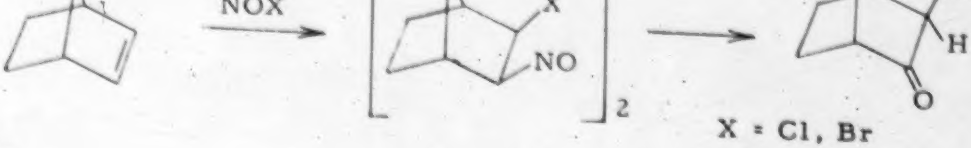
6a

6b

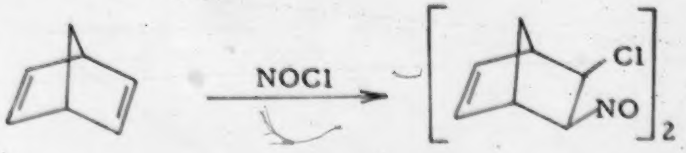
6c

Kaplan et al.[47] have suggested that nitrosyl chloride ionizes to give the nitrosonium ion (NO^+), which adds to an olefin to give a highly stabilized onium ion intermediate, 6a-c, which should open to a trans nitrosochloride.

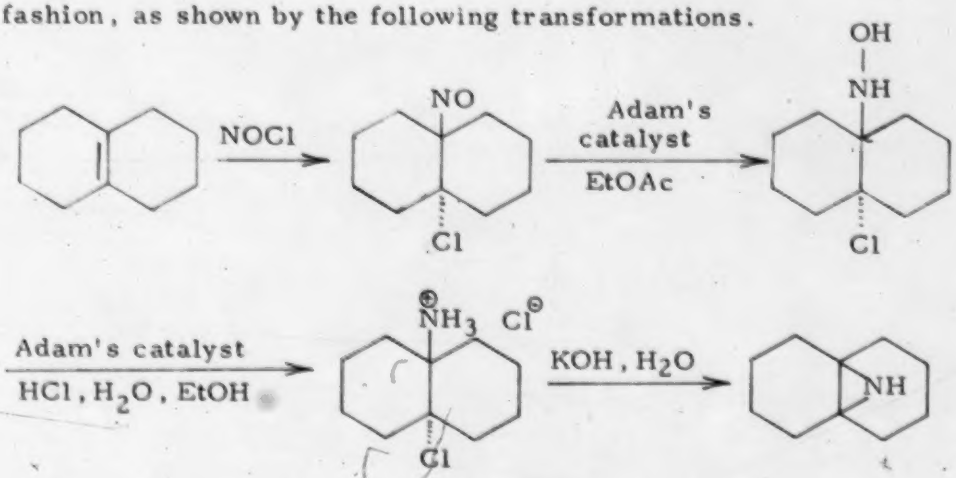
Meinwald et al.[48] have investigated the addition of nitrosyl chloride and nitrosyl bromide to norbornene, norbornadiene, endo-5-norbornenecarboxylic acid and Δ^9-octalin, with a view to elucidating the steric course of nitrosyl halide additions. Since the addition occurs without rearrangement to norbornene and norbornadiene, and no lactonic product is formed from the unsaturated acid, very little carbonium ion character is developed in the intermediate. The cis-exo- nature of the adduct is established by levulinic acid hydroylsis of the adduct.



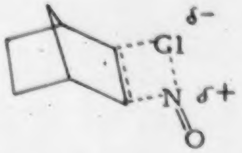
X = Cl, Br



Thus the additon of nitrosyl chloride and bromide to a number of norbornenes gives cis-exo- adducts, even where good opportunities for other reaction paths were provided. In contrast, addition of nitrosyl chloride to Δ^9-octalin proceeds in the trans-fashion, as shown by the following transformations.


NOCl
NO
Cl
Adam's catalyst
EtOAc
OH
NH
Cl
Adam's catalyst
HCl, H$_2$O, EtOH
$\overset{\oplus}{N}H_3$ Cl$^{\ominus}$
Cl
KOH, H$_2$O
NH

Thus, the steric course of nitrosyl halide addition to olefins depends on the olefin structure. Δ^9-Octalin and most other unstrained olefins give a trans- adduct in accord with the ionic reaction mechanism. On the other hand norbornene and norbornadiene undergo addition by a four-centre concerted mechanism.



The stereochemical course of nitrosyl chloride addition is solvent dependent, as shown by the fact that reaction of nitrosyl chloride with cyclohexene gives a trans- adduct in carbon tetrachloride and cis- adduct in liquid sulfur dioxide[49].

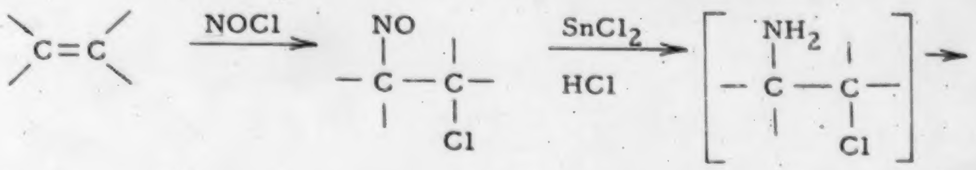
Kinetic evidence for the operation of a polar mechanism for the addition of nitrosyl halides has been obtained[50]. The reaction followed the simple kinetic form:

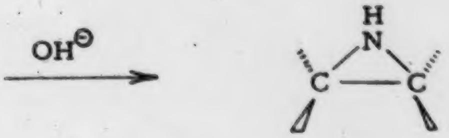
$$\frac{-d\,[\mathrm{NOCl}]}{dt} = k_2\,[\mathrm{olefin}]\;[\mathrm{NOCl}]$$

The relative rates of reaction in chloroform were shown to be consistent with the view that the reaction involves electrophilic attack by $\overset{\delta+}{\mathrm{NO}}-\overset{\delta-}{\mathrm{Cl}}$. Electron releasing methyl and phenyl groups facilitated the reaction and electron-withdrawing groups such as chlorine retarded it. On the whole, the reaction was faster in polar solvents. Similarly, evidence for a cyclic four-centre concerted mechanism has been obtained[51] from rate studies for the addition of nitrosyl chloride to linear aliphatic and cycloolefins and substituted styrenes.

In the presence of light, which facilitates the dissociation of nitrosyl halides, a free radical mechanism may also be operative; as shown by Park et al.[52], that an ionic mechanism is untenable for the reaction of nitrosyl chloride with fluoroolefins in the presence of ferric ions and light. Instances of nitrosyl bromide addition, involving the initial break-up of the pseudohalogen to NO_2, Br_2 and N_2 have also been reported[53].

Addition of nitrosyl chloride to a tetra-substituted olefin provides a convenient method for the preparation of aziridine[54], by the following sequence. Similarly, addition of nitrosyl chloride to





olefins, followed by levulinic acid hydrolysis of the adduct has been generalized as a synthetic route to α-chloroketones[22].

Nitryl chloride can add to olefins and evidence tends towards a free radical mechanism, although in aromatic substitution reactions, in the presence of Friedel-Crafts catalysts, substitution takes place to some extent through $\overset{\delta+}{NO_2}-\overset{\delta-}{Cl}$[55]. Vinyl bromide has been shown to give 1-bromo-1-chloro-2-nitroethane, 7, in good yield. Although this orientational result is consistent with a heterolytic

$$CH_2{=}CHBr \quad + \quad NO_2Cl \longrightarrow O_2NCH_2{-}CHBrCl$$

7

mechanism, it was shown that the nitro group always appeared in the terminal position regardless of the electronic effects of the substituents around the double bond. This effect prevails through a series of derivatives of acrylic acid, and with an α-methyl group[56]. Several other examples of nitryl chloride additions have been reported and the main products are usually a 1,2-chloronitro adduct and a pseudonitrosite. In many cases the reaction is complicated by addition of the elements of chlorine, nitrogen sesquioxide or nitrogen dioxide depending upon the solvent used and the olefin studied[57]. Shechter et. al.[58] from their studies on the addition of nitryl chloride to methyl acrylate postulated a mechanism involving free radicals. Recent reports on the addition of nitryl chloride to steroids[43b] and acetylenes[45] have also been published, which is consistent with the disproportionation of nitryl chloride[59] as follows:

$$2\ NO_2Cl \rightleftharpoons N_2O_4 + Cl_2$$

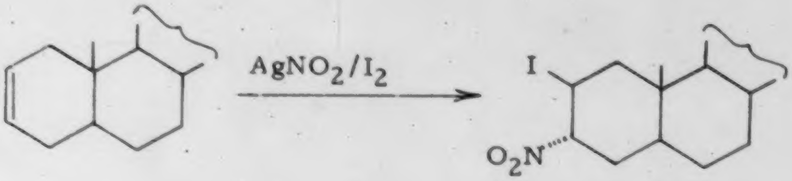
$$N_2O_4 \longrightarrow NO^+ + NO_3^-$$

$$N_2O_4 \longrightarrow N_2O_3 + \text{oxidation}$$

$$Cl_2 + N_2O_4 \longrightarrow ClNO_3 + NOCl$$

Recently, Beger[60], from his studies on the reaction between olefins and nitryl chloride has pointed out that the addition takes place by a radical mechanism in slightly polar solvents and by Cl^+ addition in polar nucleophilic solvents.

The reaction of silver nitrite with iodine is expected to lead to INO_2. This reagent is theoretically capable of dual heterolysis to NO_2^+ and I^- or to I^+ and NO_2^- as well as to homolysis into free radicals and hence it can function as nitryl iodide or as iodine nitrite and either by an ionic pathway or homolytically. The chemistry of this reagent has been studied by Hassner et al.[21] With 2-cholestene, the major product was 2β-iodo-3α-nitrocholestane 8. This suggests that the pseudohalogen was not reacting as iodine nitrite (INO_2), but instead had behaved as nitryl iodide, which was confirmed by the regiochemistry of its reaction with styrene.



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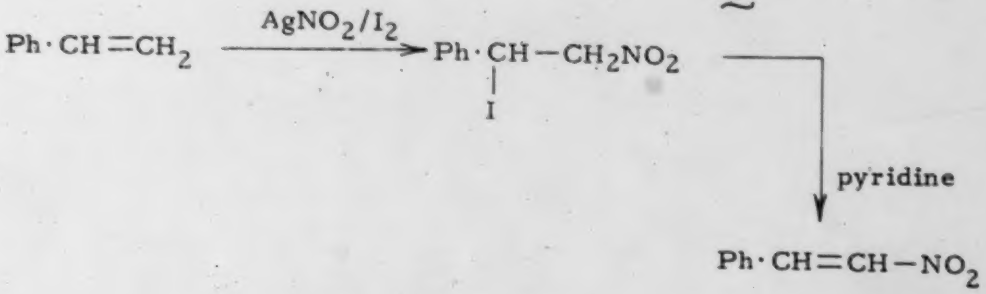
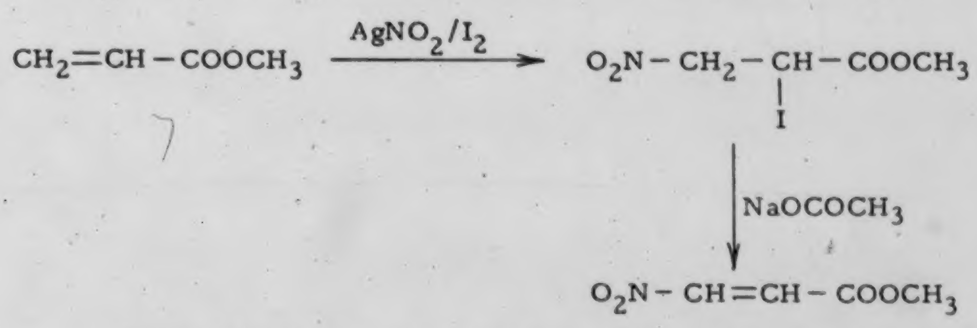


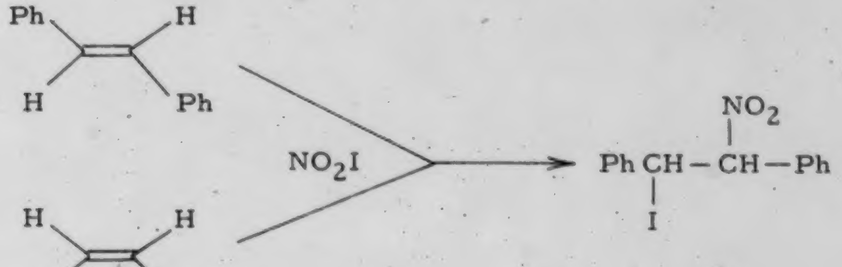
$$Ph\cdot CH{=}CH_2 \xrightarrow{AgNO_2/I_2} Ph\cdot \underset{I}{\underset{|}{C}}H - CH_2NO_2 \xrightarrow{\text{pyridine}} Ph\cdot CH{=}CH - NO_2$$

The reaction proceeds by a free radical mechanism, the nitro radical being the initial attacking species as shown by its reaction with methyl acrylate and by the inhibition of the reaction by oxygen.

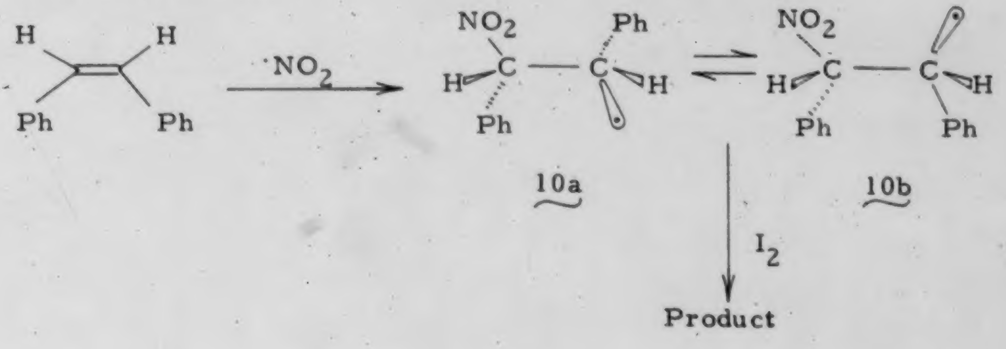


$$\mathrm{CH_2{=}CH-COOCH_3} \xrightarrow{\mathrm{AgNO_2/I_2}} \mathrm{O_2N-CH_2-\underset{\displaystyle I}{CH}-COOCH_3} \xrightarrow{\mathrm{NaOCOCH_3}} \mathrm{O_2N-CH{=}CH-COOCH_3}$$

Racemization occurs at the benzylic position as shown by the reaction of nitryl iodide with *cis* and *trans*-stilbenes. The product in both cases was a diastereomeric mixture 9, formed through the phenyl-stabilized nitroradicals 10a and 10b, which are interconvertible. The formation of the nitro radical is non-reversible, because *cis*-stilbene did not isomerize, when an excess of *cis*-stilbene was treated with nitryl iodide.

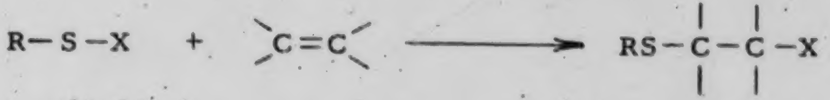

Ph
H
H
Ph
H
H
Ph
Ph
NO₂I
NO₂
Ph CH — CH — Ph
I

9


H
H
Ph
Ph
·NO₂
NO₂
Ph
H
C
C
H
Ph
NO₂
H
C
C
H
Ph
Ph
10a
10b
I₂
Product

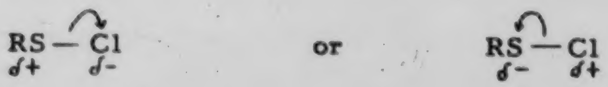
Sulfenyl halides

The sulfenyl halides easily add across olefinic bonds. Several reviews dealing with sulfenyl halide chemistry have been



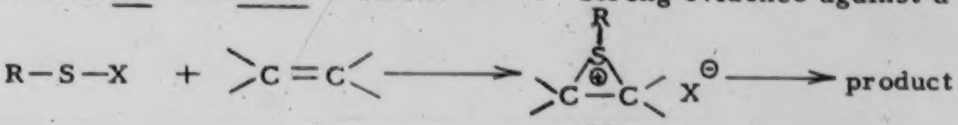
published[61-64].

The molecule R-S-Cl could in theory react in two distinct ways, either as a source of electrophilic sulfur or as a source of electrophilic chlorine[62]. Freezing point depression studies[65] with



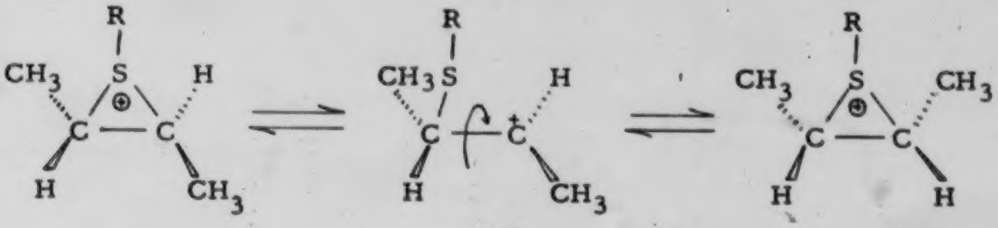
2,4-dinitrobenzenesulfenyl chloride in sulfuric acid indicates the formation of ArS^+ ion. No evidence was found to suggest that the reagent could become a source of positive chlorine.

The polar addition of sulfenyl chloride to olefins proceeds through a thiiranium ion intermediate[64], 11, support for which comes from the almost exclusive *trans*-stereospecific addition of sulfenyl chloride to *cis*- and *trans*-2-butene[66-68]. Strong evidence against a



11

non-rotating open carbonium ion, 12, has recently been supplied by the stereospecific uniformity of this addition over a wide temperature



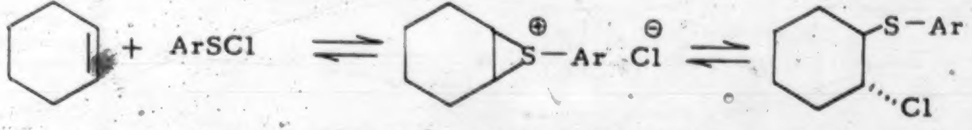
12

range[69].

The kinetics of the reaction of 2,4-dinitrobenzenesulfenyl chloride and bromide with styrene and cyclohexene has been investigated by Kharasch et al.[70,71]. They found that the reaction is of second order. Polar solvents enhanced the rate. A positive salt effect was

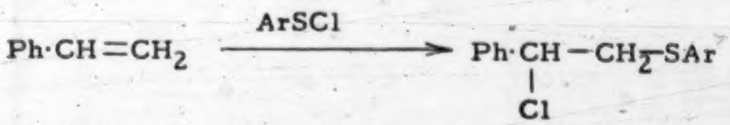
$$-\frac{d\ \mathrm{RSX}}{dt} = k\,[\mathrm{RSX}][\mathrm{Olefin}]$$

also observed. The sum of the kinetic evidence is consistent with the development of charge in the rate-determining transition state, but does not imply a thiiranium ion intermediate. Convincing evidence for a thiiranium ion intermediate has recently been supplied by Brown and Hogg[72] from an examination of the reaction rates of addition of several para-substituted ortho-nitrobenzenesulfenyl chlorides to cyclohexene. A rate limiting first step involving a transition state closely resembling the thiiranium ion was invoked to explain the sign



and magnitude of the observed ρ values. This has been further substantiated[73] by the considerably lower sensitivity of methane sulfenyl chloride additions to the electronic environment of the double bond.

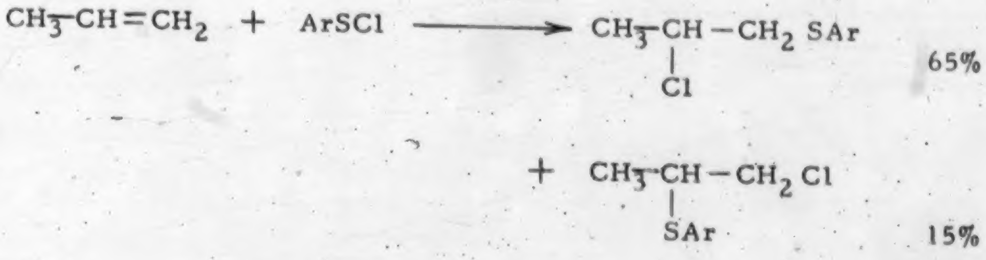
The orientation of addition is nearly exclusively in the Markovnikov sense for phenyl substituted olefins[71]. No racemization of allylic or benzylic centers is encountered, thus strongly supporting



$$\mathrm{Ph{\cdot}CH{=}CH_2} \xrightarrow{\mathrm{ArSCl}} \mathrm{Ph{\cdot}\underset{\displaystyle Cl}{\underset{|}{C}H}{-}CH_2{-}SAr}$$

sulfur bridging to the exclusion of contributions from allylic or benzylic carbonium ions. Thus conjugated dienes give exclusively the kinetically controlled 1,2-adducts[74].

Steric factors play an important role in sulfenyl halide additions as shown by the addition to propene, which also gives the kinetically controlled anti-Markovnikov adduct 13 in small but significant amount[75].



$$CH_3-CH=CH_2 + ArSCl \longrightarrow CH_3-\underset{\displaystyle Cl}{\underset{|}{CH}}-CH_2SAr \qquad 65\%$$

$$+\ CH_3-\underset{\displaystyle SAr}{\underset{|}{CH}}-CH_2Cl \qquad 15\%$$

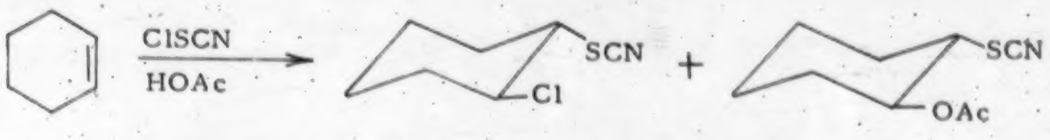
13

The stereochemistry of the addition has been well established[66,68]. It proceeds almost exclusively in the trans-sense, a result which has been taken as evidence that the entering sulfur atom is bound to both of the olefinic carbon atoms until the reaction is complete.

Many other sulfenyl halides will behave in a similar way, though there have been few mechanistic investigations of their behaviour. It is possible[76] that some of these reactions can proceed by free radical as well as by ionic mechanisms. Aryl sulfenyl bromides[77] can under certain circumstances act as sources of either electrophilic sulfur or electrophilic bromine. So with this compound the two opposed modes of polarization seem to be more nearly balanced than with the chloride.

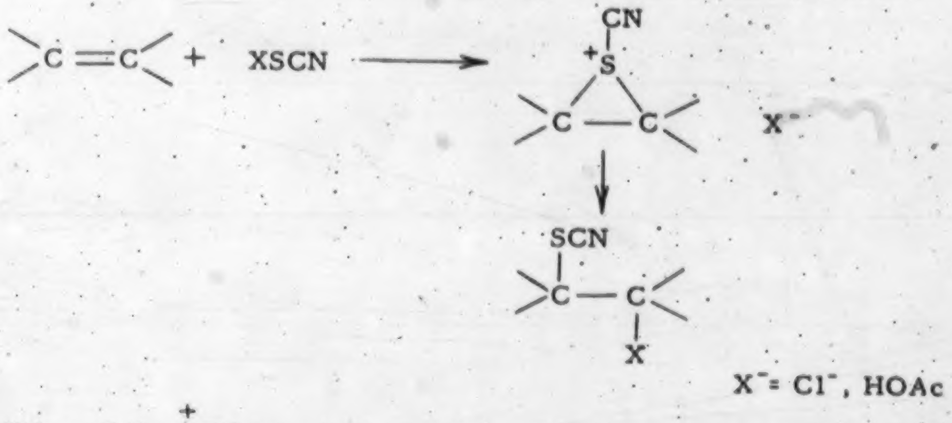
Thiocyanogen halides

The thiocyanogen halides, can all act as electrophilic regents supply the SCN group electrophilically with the positive charge developing most readily on the sulfur atom. Thiocyanogen chloride, which can be generated from lead thiocyanate and chlorine[78], gives with olefins α-chloro-β-thiocyanates in chloroform or toluene under heterolytic conditions[79,80]. In acetic acid α-chloro-β-thiocyanates and α-acetoxy-β-thiocyanates are the products[81].



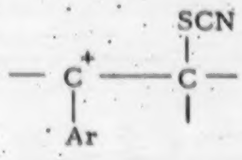
The addition is stereospecifically *trans*, as shown by the stereospecific formation of *erythro* and *threo* products from *trans* and *cis*-2-butenes respectively. With symmetrical aryl alkenes, the reaction is *trans* stereoselective. The rate of addition is enhanced by polar solvents and electron-donating substituents on the olefinic carbons. No addition occurs with olefins containing electron withdrawing substituents.

On the basis of these observations an electrophilic reaction mechanism is postulated. The electrophilic reagent adds in a two step kinetically controlled reaction, in which the first step is the



addition of the $\overset{+}{\text{SCN}}$ ion. The cyclic sulfonium ion can undergo opening from the back side, which explains the observed *trans* stereochemistry.

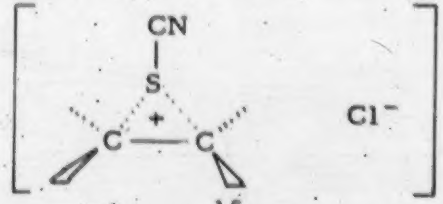
The non-stereospecific Markovnikov addition to olefins with α-aryl substituents indicates the formation of the open carbonium ion, 14:



$$-\underset{\underset{Ar}{|}}{\overset{+}{C}}-\overset{\overset{SCN}{|}}{\underset{|}{C}}-$$

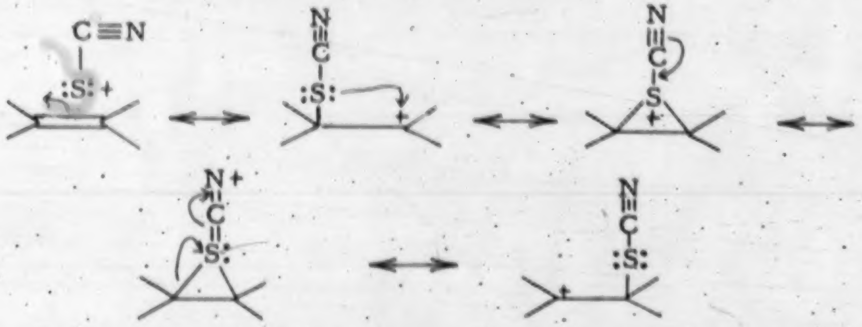
14

due to the greater stabilizing effect of the substituent. In acetic acid solvent, the sulfonium ion intermediate can be in the form of an ion pair, 15, which is appropriate for weakly dissociating solvents such as



15

acetic acid. The stability of the sulfonium ion is attributed to delocalization of the positive charge as shown below:



The stereoselectivity observed in the addition of thiocyanogen chloride to symmetrical α-aryl alkenes has been explained as due to steric control of the reaction by the thiocyanato group of the carbonium ion.

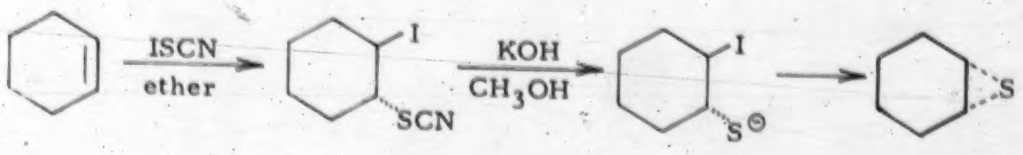
There has not been much work done on the addition of iodine thiocyanate to unsaturated compounds. Raby[83,84] has shown that iodine thiocyanate prepared by the reaction of equimolar quantities of thiocyanogen and iodine, can add to ethylenic double bonds. Acyclic and cyclic monoethylenic and non-conjugated diethylenic compounds add iodine thiocyanate normally. Conjugated dienes form only mono addition products. Electron withdrawing groups, as well as aromatic residues on both carbon atoms, either reduce the reaction rate or even inhibit it. With acetylenic compounds unstable mono addition products are formed[85]. The reaction has been explained by ionization as well as dissociation of the iodine thiocyanate molecule. Recently,

$$\mathrm{ISCN} \longrightarrow \mathrm{SCN}^{+} + \mathrm{I}^{-}$$

$$2\ \mathrm{ISCN} \longrightarrow (\mathrm{SCN})_2 + \mathrm{I}_2$$

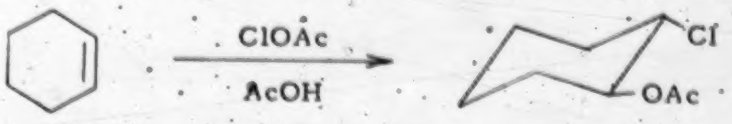
Collin et. al.[51] has obtained kinetic evidence for the electrophilic nature of the addition of iodine thiocyanate to olefins.

Addition of iodine thiocyanate, followed by basic hydrolysis of the β-iodothiocyanates, has been developed as a route to episulfides from cyclic olefins[26].



Chlorine acetate

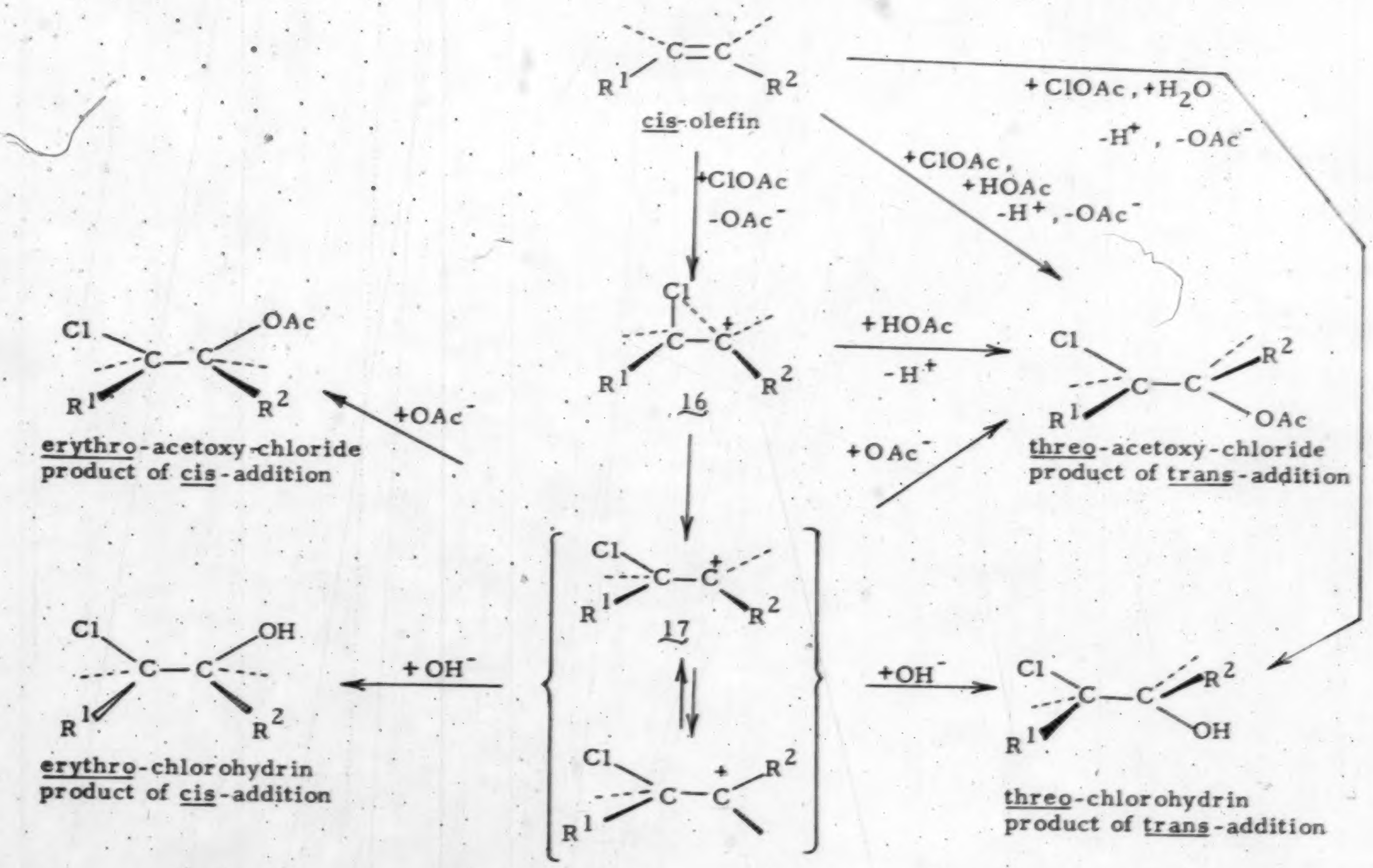
Chlorine acetate, prepared by the reaction between mercuric acetate and chlorine in anhydrous acetic acid adds to olefinic double bonds to provide acetoxy chlorides[86]. Inclusion of sufficient



amount of water in the reaction medium gives the corresponding chlorohydrins also. De la Mare et al.[86] have investigated the addition of chlorine acetate to cyclohexene, phenanthrene, acenaphthylene and a series of *cis* and *trans* *para* substituted methyl cinnamates to gain information on the stereochemistry and mechanism of addition of this reagent. With substituted methyl cinnamates, the addition is in the Markovnikov sense, and the products of reverse orientation are formed in less than 5% yield. For both *cis* and *trans* isomers, the *erythro* product is favored, except for methyl *para*-nitro-*cis*-cinnamate. The products isolated are all formed under kinetic control, and no *cis*-*trans* isomerization of olefins takes place under the reaction conditions. Cyclohexene with chlorine acetate in acetic acid gives only *trans*-1-acetoxy-2-chlorocyclohexane, whereas acenaphthylene and phenanthrene give products of both *cis* and *trans* additions.

On the basis of their observations, they proposed a reaction path as shown in Scheme 1, and the results are explained in terms of the following pathways for the formation of acetoxy chlorides.
1. Cyclohexene adopts the path via the bridged intermediate **16** to the product of *trans* addition. 2. Acenaphthylene and phenanthrene require the opening of the bridge, thus giving the intermediate **17** (open ion) to allow for the formation of both *cis* and *trans* acetoxy chlorides. 3. Methyl *trans* and *cis* cinnamates also require conversion of the intermediate **17** into its conformational isomer, so that *erythro* and *threo* acetoxy chlorides can be obtained from the two isomers in similar proportions. 4. Because of the greater importance of bridging in the intermediate derived from methyl *para*-nitro-*trans*-cinnamate, this compound makes rather greater use of reaction directly from the bridged ion 16. 5. Termolecular pathways using a component

Scheme 1

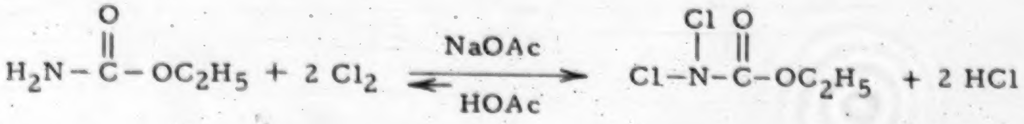

cis-olefin
+ClOAc
-OAc⁻
+ClOAc, +H₂O
-H⁺, -OAc⁻
+ClOAc,
+HOAc
-H⁺, -OAc⁻
16
+HOAc
-H⁺
+OAc⁻
17
+OH⁻
erythro-acetoxy-chloride
product of cis-addition
threo-acetoxy-chloride
product of trans-addition
erythro-chlorohydrin
product of cis-addition
threo-chlorohydrin
product of trans-addition

Proposed reaction paths in additions to some olefinic substances iniated by molecular chlorine. For routes indicated as involving OAc^- or OH^-, the alternative possible involvement of HOAc or H_2O is postulated also.

of the solvent as the nucleophile are possibly involved, particularly in the formation of chlorohydrins from relatively reactive olefins.

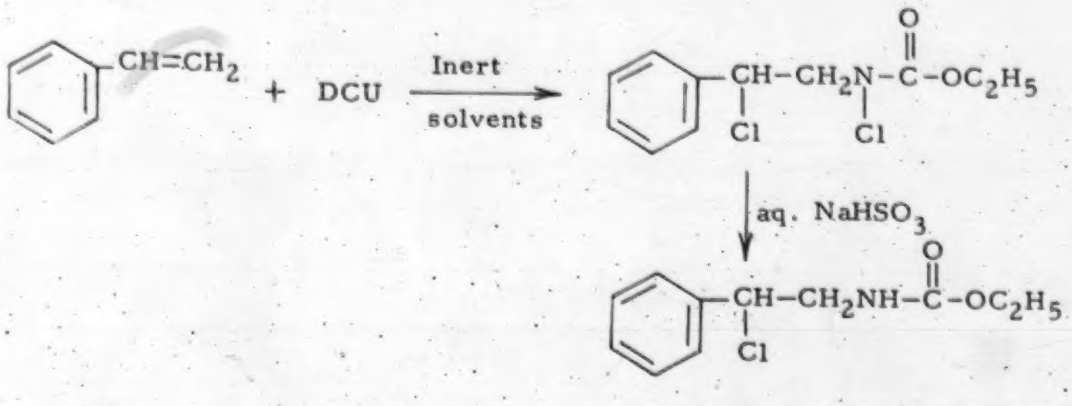
N,N-Dichlorourethan (DCU)

A pseudohalogen of considerable versatility is N,N-dichlorourethan (DCU) prepared in good yield by reaction of chlorine with urethan in buffered aqueous solution[87]. It is a highly reactive pseudohalogen in adding to double bonds[87,88]. DCU adds to many unsaturated



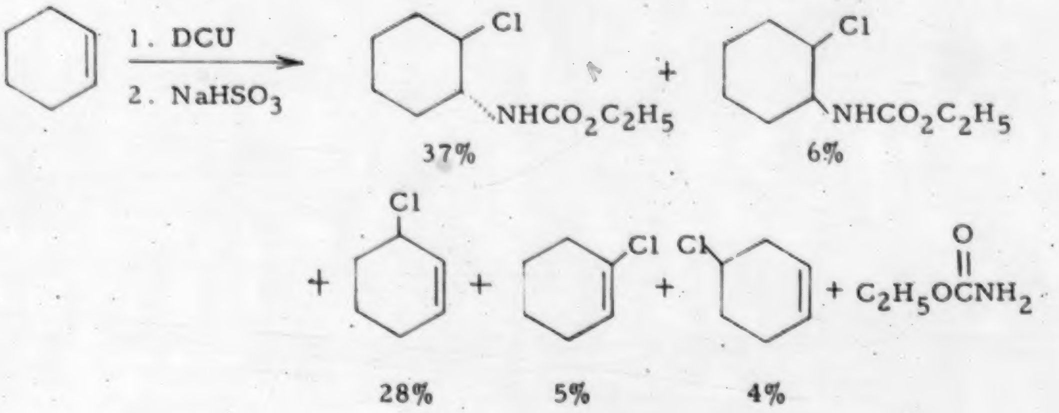
$$H_2N-\overset{\overset{O}{\|}}{C}-OC_2H_5 + 2\,Cl_2 \underset{HOAc}{\overset{NaOAc}{\rightleftarrows}} Cl-\overset{\overset{Cl}{|}}{N}-\overset{\overset{O}{\|}}{C}-OC_2H_5 + 2\,HCl$$

compounds to give N-chloro adducts, which are converted into β-chlorocarbamates by washing with aqueous sodium bisulfite solution.



The reaction proceeds well with other terminal olefins, vinyl monomers and cyclic olefins[87,89].

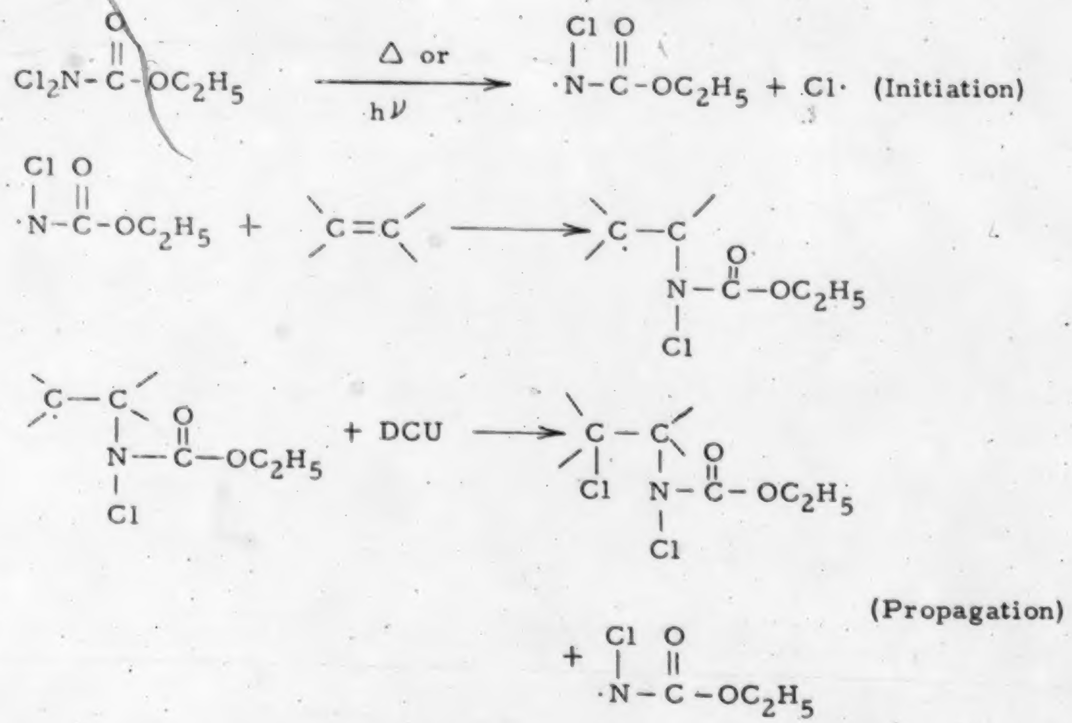
With terminal olefins and vinyl monomers, addition proceeds in an anti-Markovnikov fashion. With internal olefins allylic chlorination competes with double bond addition and mixtures of *threo* and *erythro* adducts are obtained from *cis* and *trans* olefins in approximately equimolar amounts. With cyclohexene, several products are obtained in addition to the chlorocarbamate. Norbornene



gives 3-chloronortricyclene as the major product by homoallylic attack along with other addition products.

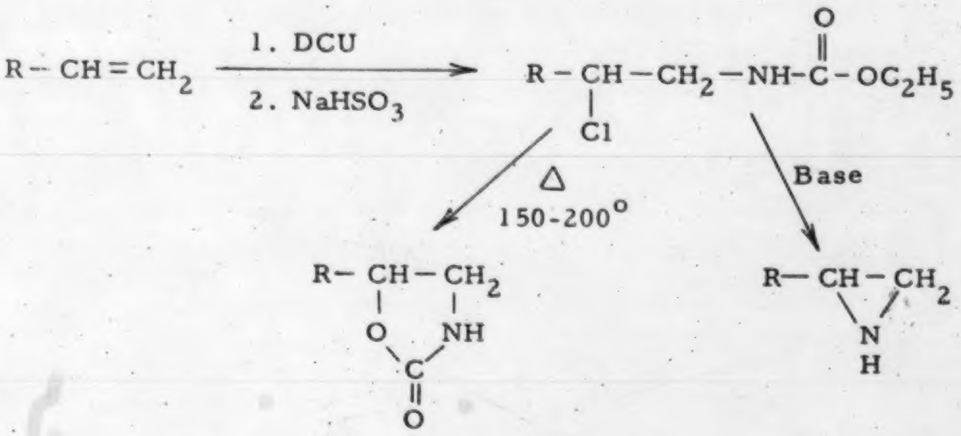
Addition of N,N-dichlorourethan to olefins is greatly affected by electronic and steric factors. Electron-withdrawing groups slow down the addition reaction, while extensive electron withdrawal completely arrests it.

The reaction has numerous characteristics of a free radical chain reaction. An induction period is observed followed by rapid exothermic reaction. Light causes a rate enhancement and free radical inhibitors slow it down. The addition is in the anti-Markovnikov fashion and is non-stereospecific. These and other factors mentioned earlier are consistent with a chain mechanism as illustrated in Scheme 2. The non-stereospecific nature of products from cyclohexene, trans-stilbene and trans-3-hexene results from free rotation of the intermediate radical before termination. Allylic attack occurs with internal olefins because the radicals formed in the initiation step have the option of adding either to the double bond or of abstracting a hydrogen atom to form a stable allylic radical, which then propagates the chain.


Δ or
hν
(Initiation)
+ DCU
(Propagation)

Scheme 2

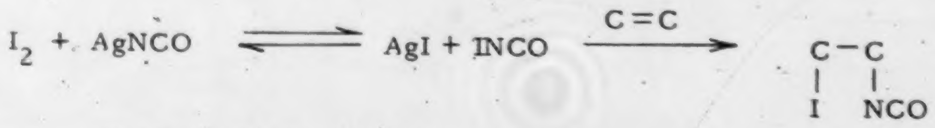
β-Chlorocarbamates are useful intermediates for the synthesis of 5-alkyl oxazolidones and aziridines[11]. (Scheme 3)


1. DCU
2. $NaHSO_3$
Δ
150-200°
Base

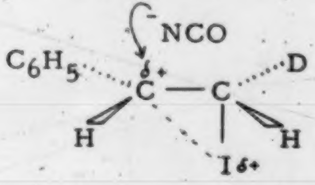
Scheme 3

Halogen isocyanates

The addition of iodine isocyanate to unsaturated substrates has been extensively studied in recent years both synthetically and mechanistically. Although bromine isocyanate and chlorine isocyanate can be obtained only as polymeric materials[90], elements of both have been added to olefins[12]. Iodine isocyanate, which can be generated in solution from iodine and silver cyanate[90], can add to olefins to afford β-iodoisocyanates. This reaction has been successfully utilized in recent years[9,10,12-14,91-101], after the initial investigation by Birkenbach and co-workers[102]. It has been demonstrated that the additions generally occur in a stereospecific manner and that the iodine and isocyanate functions are introduced trans to each other and diaxially in rigid fused cyclohexanes[9]. These results have been interpreted as the formation of a three-membered ring iodonium ion intermediate which was opened from the back side by isocyanate ion[94] and which for aryl substituted olefins can adopt the unsymmetrically bridged form 18.

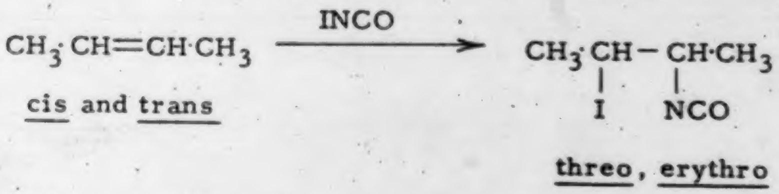


$$I_2 + AgNCO \rightleftharpoons AgI + INCO \xrightarrow{C=C} \underset{I}{C}-\underset{NCO}{C}$$



18

Thus cis and trans 2-butenes give threo and erythro iodo-isocyanate adducts respectively. The stereospecific trans addition and the

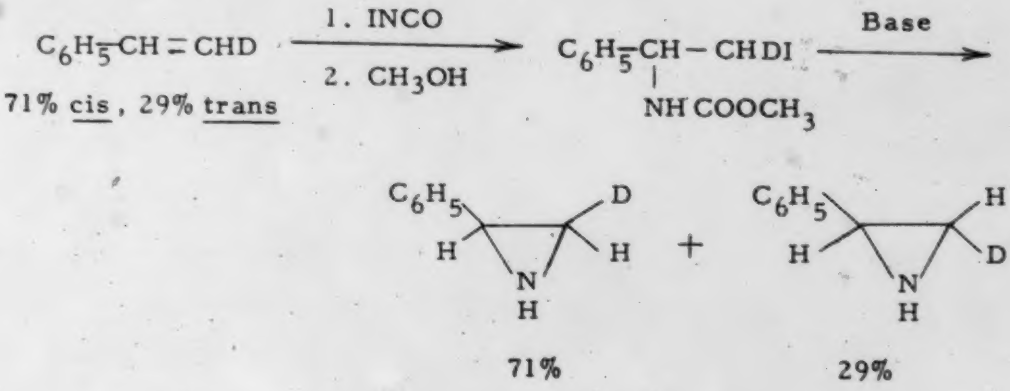


$$CH_3\cdot CH{=}CH\cdot CH_3 \xrightarrow{INCO} CH_3\cdot\underset{I}{CH}-\underset{NCO}{CH}\cdot CH_3$$

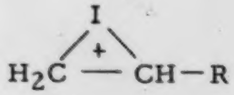
cis and trans

threo, erythro

non-involvement of a benzylic carbonium ion in the case of unsymmetrical arenes were proven by addition of iodine isocyanate to β-deuterostyrene[96].

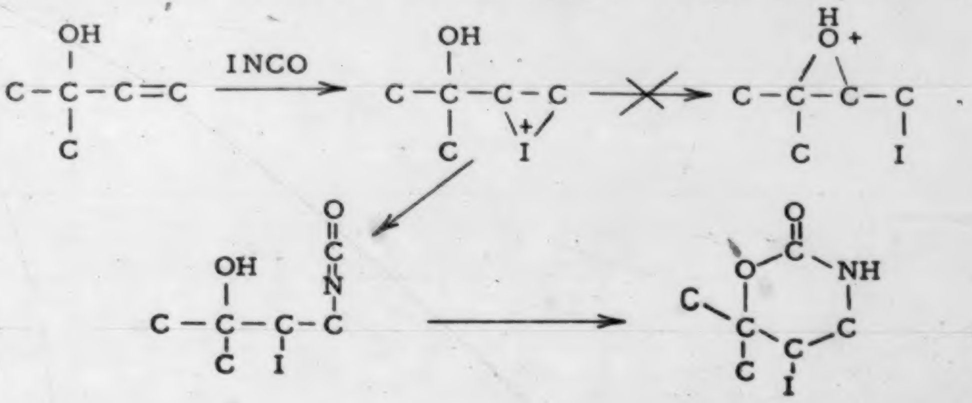


The addition of iodine isocyanate to styrene is not only stereospecific (trans), but also regiospecific (NCO-phenyl). But one can visualize cases in which the nature of the R group in 19, would



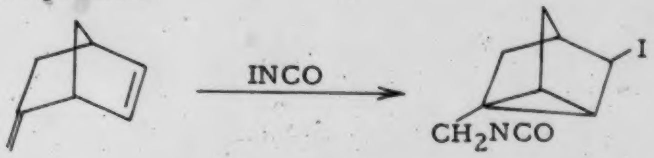
19

influence the regiochemistry of INCO additions in a different sense. Thus 1-hexene reacts with iodine isocyanate to give a 70:30 mixture of secondary and primary isocyanates. Tert.-butylethylene gives the primary isocyanate as the exclusive product, indicating the steric requirements for the attack of isocyanate anion. Absence of participation by a neighboring hydroxy-group is shown by the addition of iodine isocyanate to 3-hydroxy-3-methyl-butene. These results show that

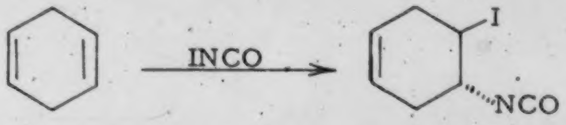


the addition of iodine isocyanate can be influenced greatly by steric factors and that no free carbonium ion is formed in these systems which would lead to skeletal rearrangements or hydroxy participation.

Addition of iodine isocyanate to norbornene, α-pinene and norbornadiene gives complex mixtures of products, in agreement with the tendency of these systems to undergo rearrangement upon the addition of electrophilic reagents. Methylene norbornene also gives a rearranged product.



Iodine isocyanate readily adds to di- and triolefins to give mono addition products[12]. Conjugated unsaturated carbonyl compounds

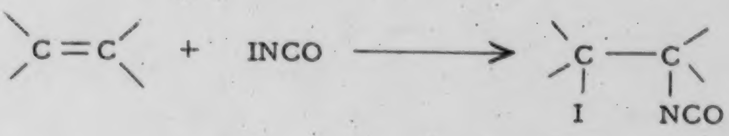


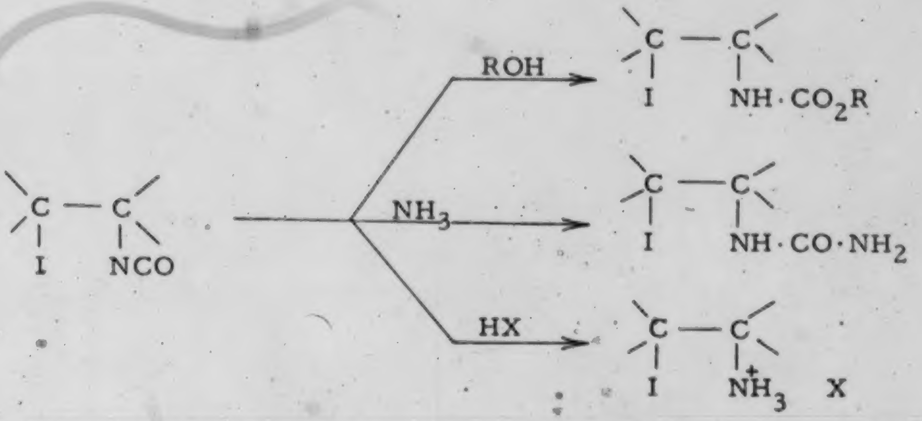
are recovered unchanged upon exposure to INCO, as are stilbene and diphenyl acetylene. Thus conjugated electronwithdrawing groups deactivate the double bond sufficiently to prevent electrophilic addition to these olefins. On the other hand INCO can add readily to conjugated dienes, monosubstituted acetylenes and allenes[101].

These studies suggest that iodine isocyanate is an electrophilic reagent. The investigations of Gebelein and Swern[97,99] and of Gebelein, Rosen and Swern[100] on the relative rates of addition of INCO to unsaturated compounds of widely varying structure and nucleophilicity confirm that conclusion. Electron donating alkyl groups attached to the double bond accelerate the rate of addition, while electron withdrawing carbonyl, chlorine and ester groups markedly retard it.

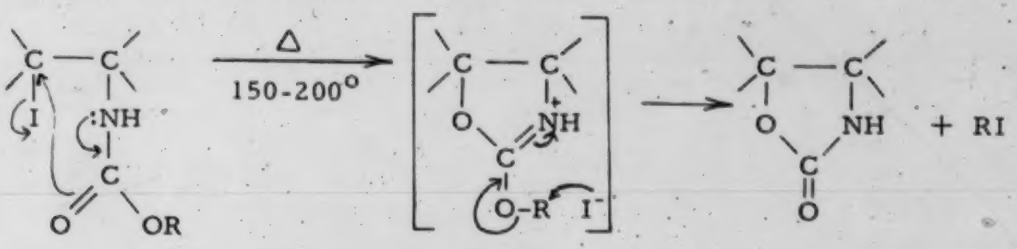
These results are in agreement with the expected stabilizing or destabilizing effect of substituents on the positive charge in an intermediate iodonium ion.

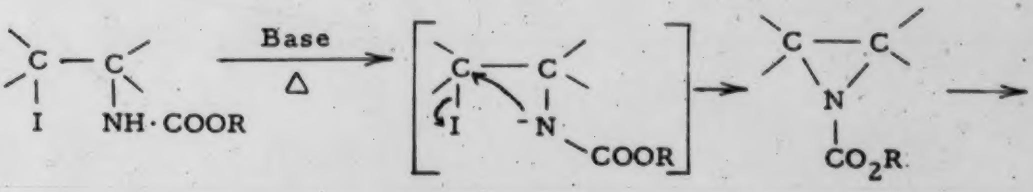
β-Iodoisocyanates are highly reactive and useful intermediates in the preparation of β-iodocarbamates, β-iodoureas and β-iodoamine hydrochlorides by reaction with alcohols, ammonia or hydrochloric acid respectively[12,99].

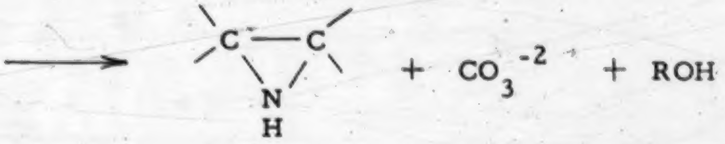

C=C
+
INCO
C—C
I
NCO


C—C
I
NCO
ROH
NH₃
HX
C—C
I
NH·CO₂R
C—C
I
NH·CO·NH₂
C—C
I
NH₃ X

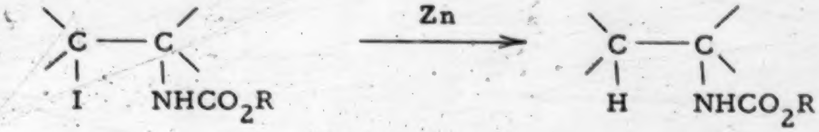
β-Iodocarbamates are readily converted to 2-oxazolidones[93] by pyrolysis and to aziridines by reaction with base[12,99]. They can


C—C
I
:NH
C
O
OR
Δ
150-200°
C—C
O
NH
C
O-R
I⁻
C—C
O
NH
C
O
+ RI


C—C
I
NH·COOR
Base
Δ
C—C
I
⁻N
COOR
C—C
N
CO₂R



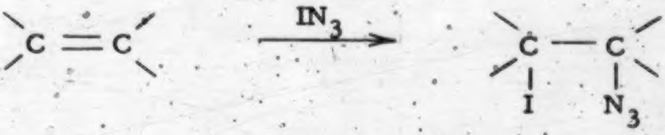
be reduced with zinc to carbamates[96].



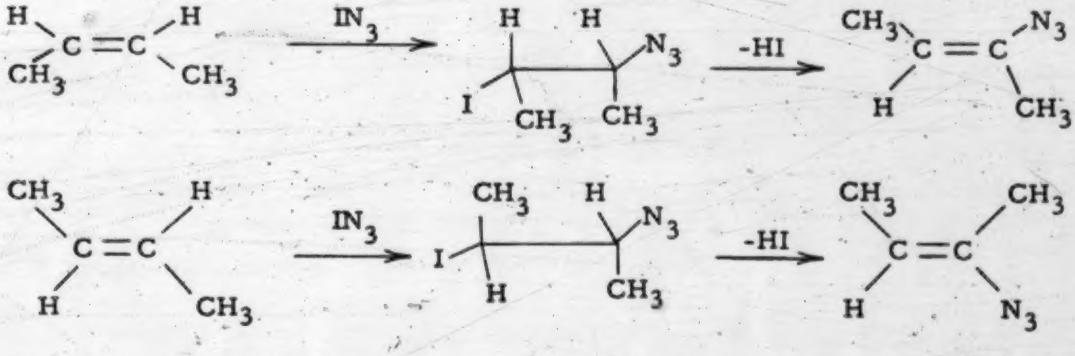
Halogen azides

The halogen azides, viz iodine azide, bromine azide and chlorine azide, represent a group of pseudohalogens which are chemically versatile and have wider synthetic scope. Iodine azide is the most important among them. Their chemistry has been largely investigated by Hassner and co-workers[1,2,103-109].

Iodine azide, generated in situ, by the reaction between sodium azide and iodine monochloride readily adds to olefins to provide β-iodoazides.

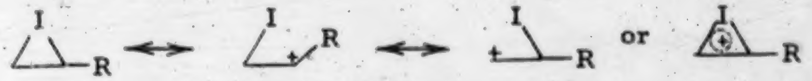


The addition of iodine azide is highly stereospecific. Thus cis and trans-2-butenes give threo and erythro β-iodoazides respectively, the configuration of which have been determined by base-catalyzed

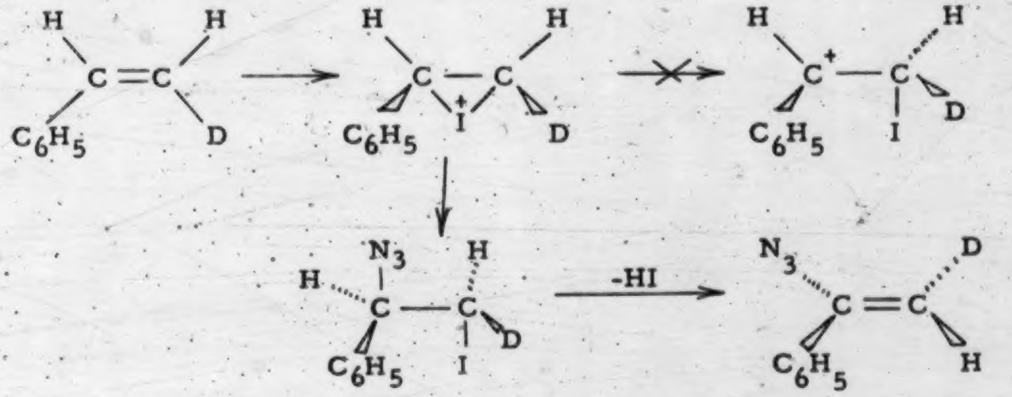


elimination of hydrogen iodide to the corresponding vinyl azides[1]. Similarly addition of iodine azide to *cis* and *trans*-stilbenes is stereospecifically *trans*. With terminal olefins, the orientation of addition is in the Markovnikov sense with the azide occupying the internal position.

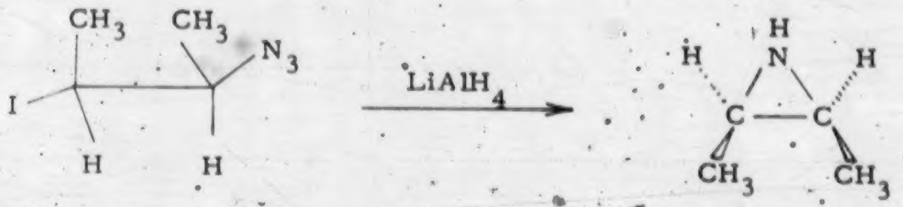
These data are consistent with an electrophilic addition, involving the intervention of a cyclic iodonium ion, which is opened up from the backside by azide ion to give the observed stereochemistry.



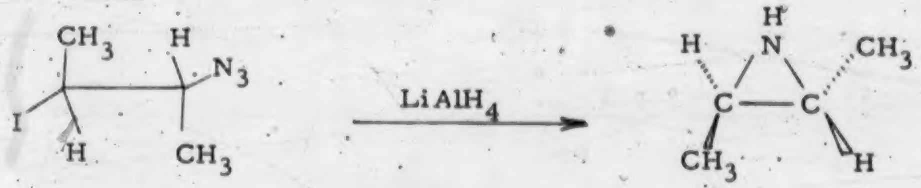
The fact that the observed *trans* stereochemistry is not due to restricted rotation in the intermediate carbonium ion in the case of aryl substituted olefins was proven[104] by addition of iodine azide to *cis*-β-deuterostyrene. This also proves the non-intervention of



benzylic cations in the addition of iodine azide to aryl substituted olefins. Additional evidence for *trans* addition is provided by the stereospecific reduction of *threo* and *erythro* β-iodoazides, obtained from *cis* and *trans* olefins respectively, to *cis* and *trans* aziridines[8].



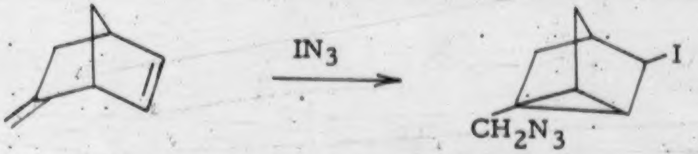
threo

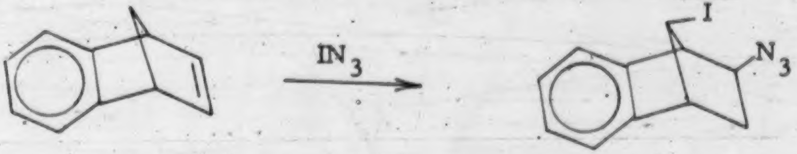


erythro

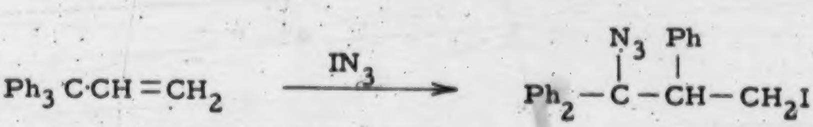
Like other pseudohalogens, addition of iodine azide is influenced by steric factors. Thus tert.-butylethylene gives the primary azide, which arises by opening of the iodonium ion at the sterically favorable, but electronically unfavorable primary position[1].

Addition of iodine azide also leads to rearrangement in those systems, where this is structurally possible. Thus methylenenorbornene and benzonorbornadiene lead to rearranged products in almost quantitative yield[106,107]. Unlike t-butylethylene, in which no





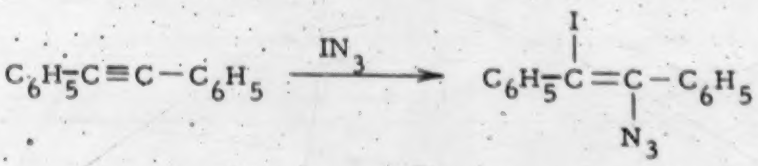
rearrangement is observed, tritylethylene reacts with iodine azide to give a product, which arises by phenyl migration. This is due to the



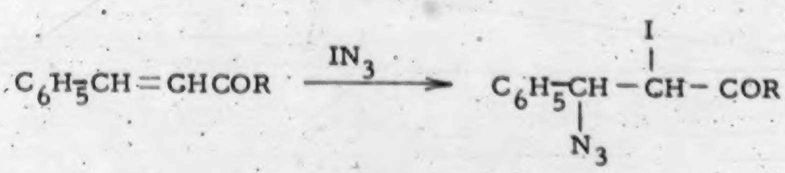
$$Ph_3C{\cdot}CH=CH_2 \xrightarrow{IN_3} Ph_2-\overset{\overset{N_3}{|}}{C}-\overset{\overset{Ph}{|}}{C}H-CH_2I$$

release of steric overcrowding as well as to the superior ability of the phenyl group to participate in the stabilization of a neighboring charge.

Unlike iodine isocyanate, iodine azide is reactive towards α,β-unsaturated ketones and esters and disubstituted acetylenes[1,109].

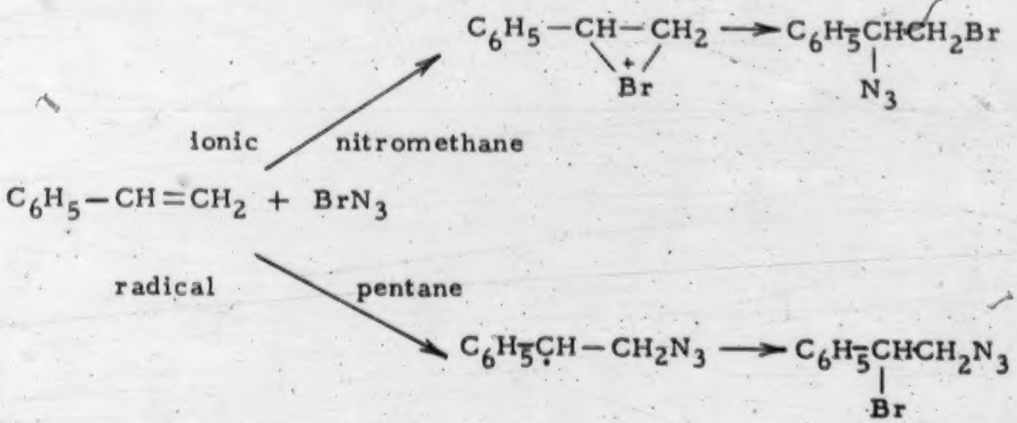


$$C_6H_5-C\equiv C-C_6H_5 \xrightarrow{IN_3} C_6H_5-\overset{I}{C}=\underset{N_3}{C}-C_6H_5$$



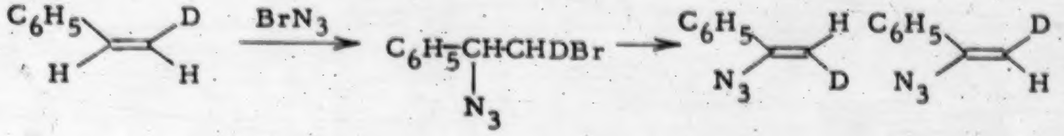
$$C_6H_5-CH=CHCOR \xrightarrow{IN_3} C_6H_5-\underset{N_3}{CH}-\overset{I}{CH}-COR$$

Bromine azide and chlorine azide differ from iodine azide in that they are capable of free radical behaviour towards olefins, since the electronegativity of chlorine and bromine is higher than that of iodine and probably also higher than that of N_3 radical. Bromine azide is capable of reacting by a dual mechanism depending upon the polarity of the solvent and/or the presence of light and oxygen[105,110]. In nitromethane, the product formed was from ionic electrophilic attack of BrN_3 on the olefin, whereas in pentane even in the absence of free radical inhibitors the reaction proceeded through attack of $N_3^{\cdot}$ on the double bond to give exclusively the opposite regioisomer. Using

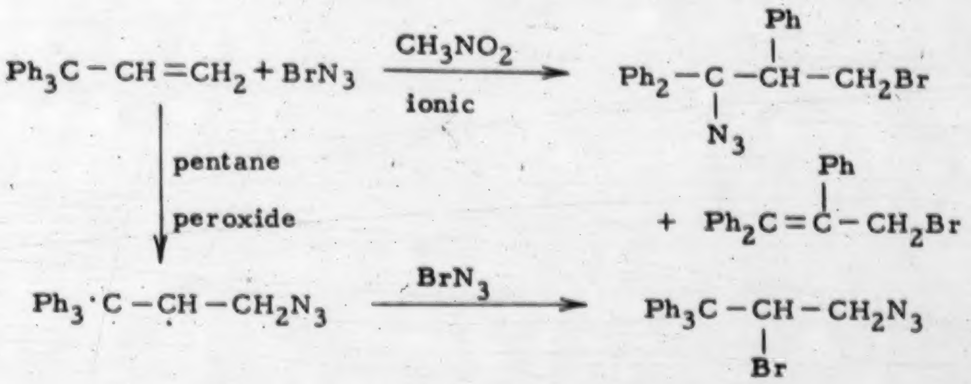


solvents of intermediate polarity variable mixtures of regioisomers were obtained.

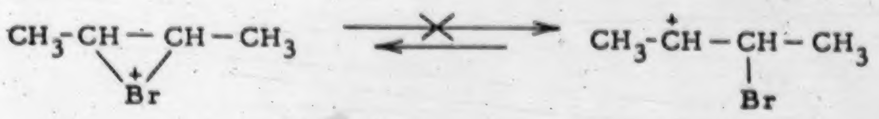
The free radical addition of BrN_3 to olefins is non-stereospecific. Thus cyclohexene gives a mixture of *cis* and *trans* adducts. The ionic addition occurs stereospecifically *trans* with alkyl substituted olefins. But with *cis*-β-deuterostyrene a mixture of products was obtained.

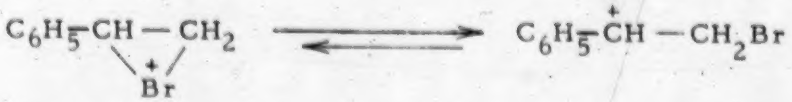

C6H5
D
H
H
BrN3
C6H5CHCHDBr
N3
C6H5
H
N3
D
C6H5
D
N3
H

Triphenylpropene, with BrN_3, gives products of phenyl migration under ionic conditions and a non-rearranged product under free radical conditions[107].


Ph3C − CH = CH2 + BrN3
CH3NO2
ionic
Ph
Ph2 − C − CH − CH2Br
N3
Ph
+ Ph2C = C − CH2Br
pentane
peroxide
Ph3·C − CH − CH2N3
BrN3
Ph3C − CH − CH2N3
Br

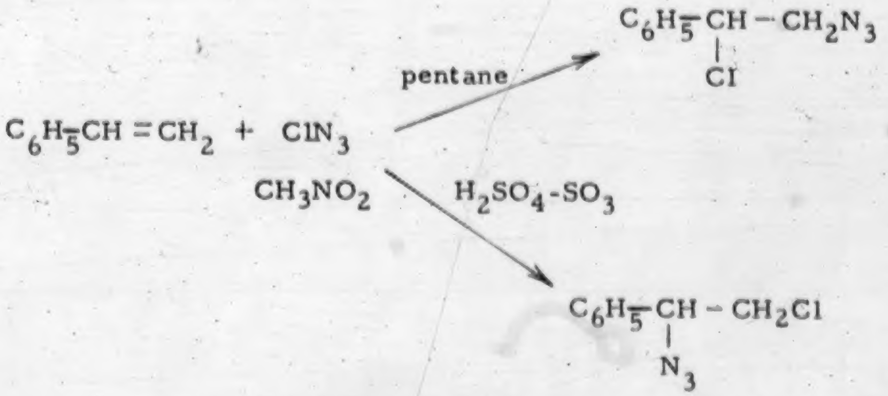
These results indicate that a three membered ring bromonium ion is stable when flanked by alkyl groups, but that even one phenyl substituent is sufficient to cause equibration to a benzyl cation.


CH3-CH − CH − CH3
Br
CH3-CH − CH − CH3
Br



$$C_6H_5-\underset{\diagdown\overset{+}{Br}\diagup}{CH-CH_2} \rightleftharpoons C_6H_5-\overset{+}{C}H-CH_2Br$$

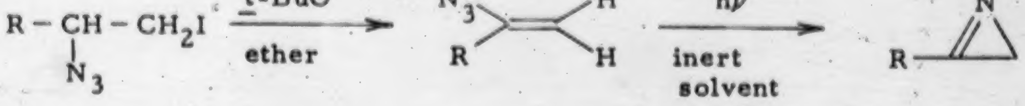
Chlorine azide, as expected, adds to olefins primarily as a free radical reagent providing a source of N_3 radicals[105,110]. Thus in pentane or methylene chloride, even in the presence of air, styrene furnishes the free radical addition product. In nitromethane, in the presence of oxygen the free radical product was still formed in 17% yield. In the presence of fuming sulfuric acid the ionic addition is the only pathway.



$C_6H_5-CH-CH_2N_3$ (Cl)
pentane
$C_6H_5CH=CH_2$ + ClN_3
CH_3NO_2
$H_2SO_4-SO_3$
$C_6H_5-CH-CH_2Cl$ (N_3)

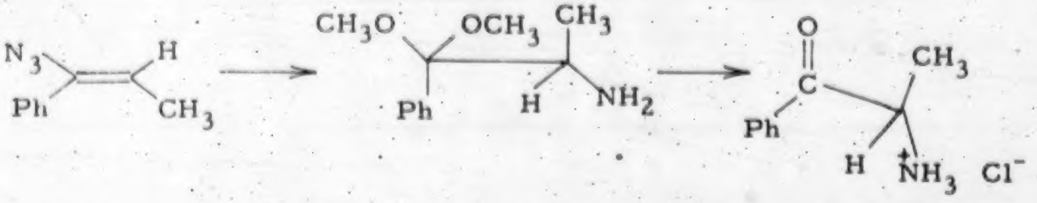
The addition of halogen azides to olefins provides a useful method for the stereospecific and regiospecific introduction of an azide function into organic molecules. The resulting β-haloalkyl azides are useful intermediates for the preparation of a number of nitrogen containing organic compounds.

Treatment of the β-haloazides with potassium t-butoxide or diazabicyclooctane (DABCO) in ether gives the vinyl azides[2-5], which can be photolysed to the 1-azirines[6,7]. The vinyl azide can

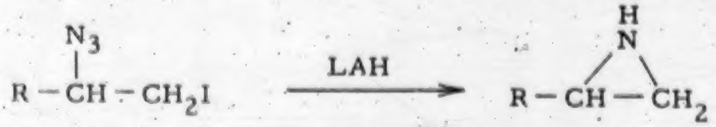


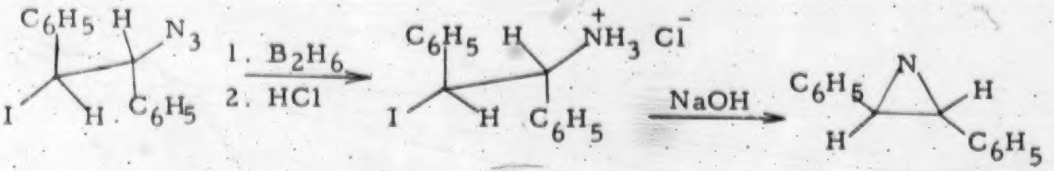
$R-CH-CH_2I$ (N_3)
t-BuO⁻
ether
N_3
R
H
H
hν
inert solvent
N
R

be photolysed in methanol in the presence of sodium methoxide to afford aminoketone dimethyl ketal, which can be hydrolysed directly to the aminoketone hydrochloride with aqueous hydrochloric acid[6].



The β-haloazides can be reduced with a variety of reducing agents to the aziridines[8]. The β-haloazides are also useful intermediates for the synthesis of several other N-heterocycles.

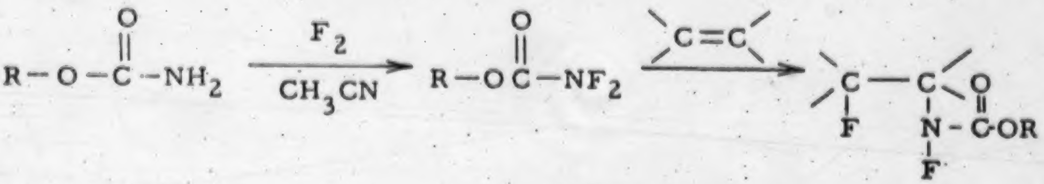




In addition to those discussed above, there are a number of other pseudohalogens which have been studied[111]. Brief mention of the chemistry of some of the most important ones may be made at this point.

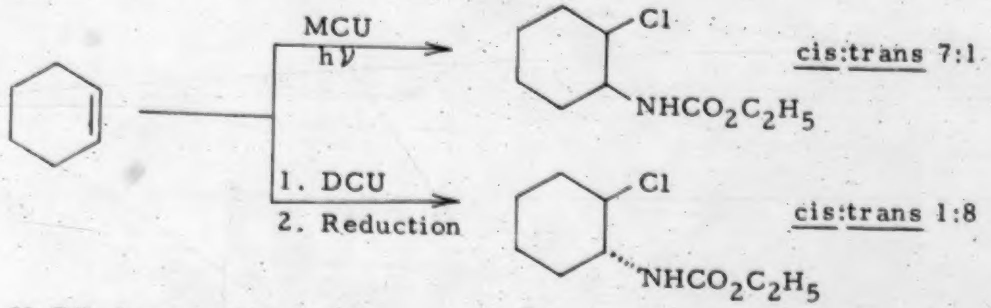
N,N-Difluorocarbamates

The alkyl N,N-difluorocarbamates, which can be prepared by the reaction of fluorine with alkyl carbamates in a suitable solvent[112], readily add to olefins (cyclohexene, cyclopentene, methyl acrylate) and thus permit ready and controlled introduction of fluorine into hydrocarbons.



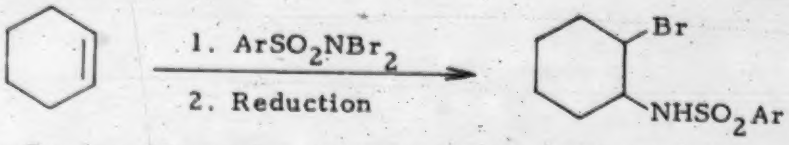
N-Monochlorourethan (MCU)

N-Monochlorourethan (MCU) does not add to double bonds under the usual reaction conditions, although it has a highly reactive positive halogen. However, in the presence of ultraviolet light, it adds readily to unsaturated[113,114] compounds to give β-chlorocarbamates in high yields. Terminal olefins preferentially give anti-Markovnikov products. An interesting feature of MCU addition is that cyclic olefins give both cis and trans addition products with the former predominating. The cyclohexene adduct, for example, has a cis:trans ratio of 7, whereas the corresponding addition of DCU gives a cis:trans ratio of about 1:8.



N,N-Dihaloarylsulfonamides

Addition of N,N-dihaloarylsulfonamides to unsaturated substrates gives mainly trans addition[115]. It is not yet known with certainty whether the addition reaction proceeds by a free radical or ionic mechanism.

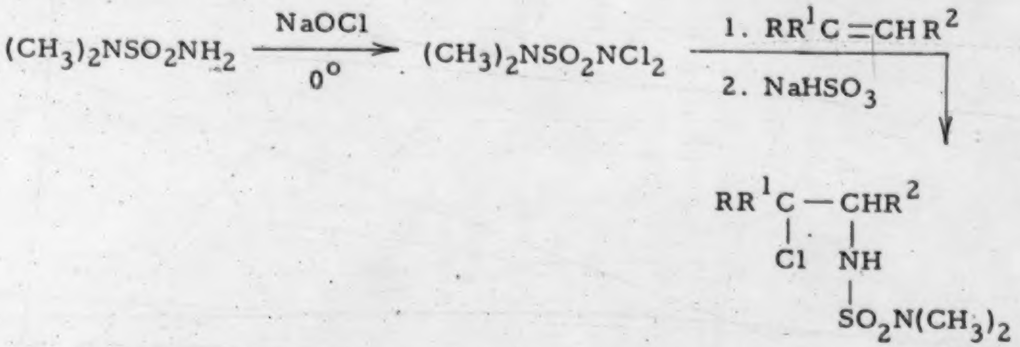


Some evidence for the ionic addition of N,N-dichloroarylsulfonamides to olefins has been reported[116] but they can apparently add either by a free radical[117] or ionic mechanism depending upon the reaction conditions.

The addition of N,N-dichloroarylsulfonamides to simple olefins is predominantly anti-Markovnikov, which is consistent with a free radical mechanism[118]. It is possible that small quantities of Markovnikov products are being formed via a competing ionic mechanism. Conjugated dienes give predominantly 1,4 addition. The reaction is strongly inhibited by oxygen indicating a free radical mechanism.

N,N-Dichloro-N',N'-dimethylsulfamide

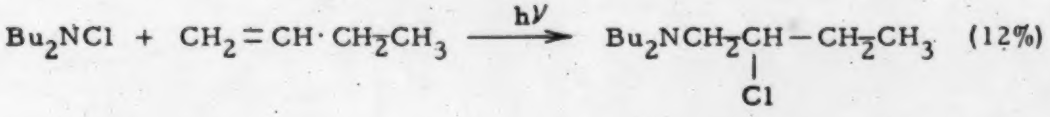
This pseudohalogen, prepared by the reaction of N,N-dimethylsulfamide with sodium hypochlorite[119], reacts exothermically with phenyl ethylenes in chloroform to give free radical addition products which can be reduced to the corresponding N-(β-chloroethyl) N,N'-dimethylsulfamides.



$$(CH_3)_2NSO_2NH_2 \xrightarrow[0^\circ]{NaOCl} (CH_3)_2NSO_2NCl_2 \xrightarrow[2.\ NaHSO_3]{1.\ RR^1C{=}CHR^2} RR^1C(Cl){-}CHR^2NHSO_2N(CH_3)_2$$

Dialkyl-N-chloroamines

The addition of N-alkyl-N-chloramines to 1,3-dienes, terminal olefins, vinyl and alkyl compounds and their unsaturated systems, in sulfuric-acetic acid media with or without u.v. illumination has been studied by Neale[120,121]. These facile free radical chain reactions all involve an addition of the aminium radical, $R_2\dot{N}H$, to a carbon-carbon multiple bond as the key step to afford 1:1 adducts. Addition, not hydrogen abstraction, is characteristic of aminium radical reactions. Some examples are given below:

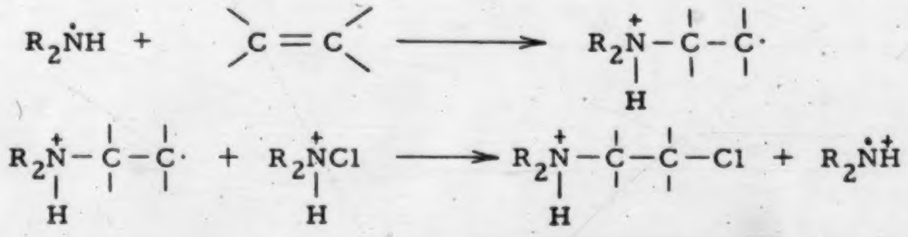


$$\mathrm{Bu_2NCl + CH_2{=}CH\cdot CH_2CH_3 \xrightarrow{h\nu} Bu_2NCH_2\underset{\underset{\displaystyle Cl}{|}}{C}H-CH_2CH_3} \quad (12\%)$$

$$\mathrm{Bu_2NCl + CH_2{=}CH-CH{=}CH_2 \xrightarrow[\substack{CH_3COOH \\ N_2,\ 10^{o}}]{\underline{4M}\ H_2SO_4} Bu_2NCH_2CH{=}CHCH_2Cl} \quad (60\%)$$

$$\mathrm{Et_2NCl + (CH_3)_2C{=}CH_2 \xrightarrow{H_2SO_4} N.R.}$$

A suggested reaction pathway is the following:



Thus the above survey clearly indicates significant differences in reactivity and the types of reactions undergone by different pseudohalogens. Differences in the mechanism of addition are also apparent among various pseudohalogens. Usually assignment of mechanistic pathway is complicated by the sensitivity of the regiochemistry of ionic additions of pseudohalogens to both electronic and steric factors[1,2].

The halogen nitrates have been known for a long time both as pure pseudohalogens and as complexes with pyridine and quinoline. Iodine nitrate and bromine nitrate were prepared by the reaction of iodine or bromine with silver nitrate in absolute methanol or ethanol[122-126]. The iodine nitrate (INO_3) was usually in equilibrium with iodine trinitrate ($I(NO_3)_3$). Other methods used to generate iodine and bromine nitrates included reaction of iodine with bromine trinitrate[127,128] and reaction of chlorine nitrate with $I(NO_3)_3$ or

INO_3-$I(NO_3)_3$ mixture or BrCl in $CFCl_3$ at low temperatures[129].

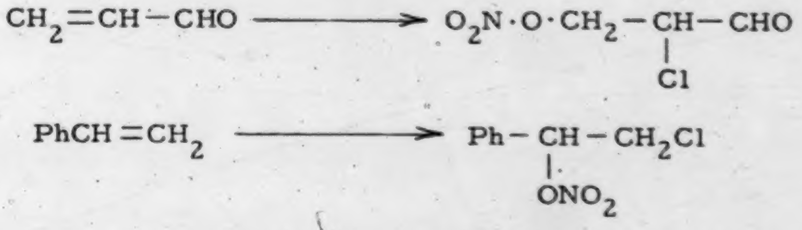
$$Br(NO_3)_3 + I_2 \xrightarrow{-50^{\circ}} BrNO_3 + 2\,INO_3$$

$$ClNO_3 + I(NO_3)_3 \longrightarrow INO_3$$

Chlorine nitrate on the other hand is prepared by the reaction of dinitrogen pentoxide with chlorine oxide (Cl_2O) in the molten state[130,131]. All the three halogen nitrates form complexes of the type, XPy_2NO_3, with pyridine[128,129,132]. The methods for iodine nitrate and bromine nitrate were not satisfactory since they can easily decompose in alcohol[123b].

$$INO_3 + CH_3OH \rightleftharpoons IOCH_3 + HNO_3$$

The only reports on the addition of these pseudohalogens to unsaturated substrates, which appeared in the literature, are reaction of iodine nitrate (INO_3) with cyclohexene to give the iodoalkyl nitrate[133] and the reaction of chlorine nitrate ($ClNO_3$) with olefins in $CFCl_3$ to give chloroalkyl nitrates[130]. It was found that the NO_3 group always entered at the more positive carbon atom.



$$CH_2{=}CH{-}CHO \longrightarrow O_2N{\cdot}O{\cdot}CH_2{-}\underset{\substack{|\\ Cl}}{CH}{-}CHO$$

$$PhCH{=}CH_2 \longrightarrow Ph{-}\underset{\substack{|\\ ONO_2}}{CH}{-}CH_2Cl$$

The chemistry of these pseudohalogens as complexes with pyridine has not been reported until recently. It was shown that iodonium nitrate ($I{\cdot}Py_2{\cdot}NO_3$) can be easily generated by the reaction of iodine monochloride with silver nitrate in chloroform-pyridine, and that it readily undergoes addition to alkenes to form (i) iodoalkyl nitrates, (ii) iodoalkyl pyridinium nitrates or (iii) alkenyl pyridinium iodides depending on the substrate[134,135]. With certain olefinic alcohols iodonium nitrate affords (iv) hydroxy-iodoalkyl nitrates and (v) hydroxy iodoalkyl pyridinium nitrates[136]. Parallel reactions in chloroform-*sym*-collidine gave three, four and five membered cyclic ethers as well as products of the type (iv) signifying neighboring hydroxy participation in contrast to the known chemistry of iodine isocyanate[96] and iodine azide[109] and differing in scope from the additions of iodine to unsaturated alcohols[137]. Iodonium nitrate in chloroform-pyridine adds to cyclohex-2-en-1-ol in a stereospecific *trans* fashion in which the iodonium ion is formed *cis* to the hydroxyl group[136]. The additions of pseudohalogens in general are quite sensitive to steric hindrance effects. So this result signified some compensating interaction between iodine and hydroxyl which was controlling the stereochemistry. This is potentially useful for the stereospecific control of the introduction of the aziridine moiety into Mytomycin analogs[138].

The scope of these and other reactions and the reactivity of iodonium nitrate were sufficiently different from those of other pseudohalogens to warrant further study. In view of the differences in reactivity and even gross mechanism noted above amongst other pseudohalogens, it was necessary to undertake an extensive physical organic study.

Hassner has observed significant differences in reactivity and mechanism for the addition of halogen azides to unsaturated substrates[105,107,110]. So it was necessary to examine the chemistry of bromonium nitrate additions to establish possible similarities or differences between the two pseudohalogens.

Vinyl pyridinium salts have been known to have significant anthelmintic activity[139]. Therefore it was of interest to us to prepare a series of iodoalkyl pyridinium nitrates and alkenyl pyridinium iodides for biological evaluation.

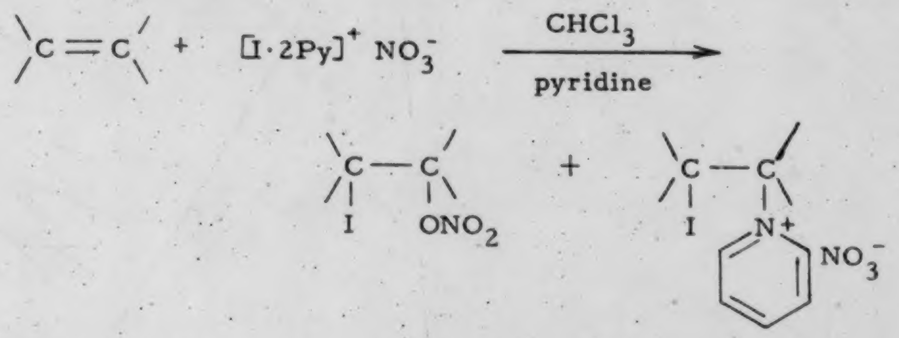
CHAPTER II

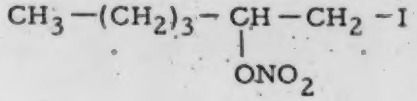
Reactions of Iodonium Nitrate with Unsaturated Hydrocarbons, α,β-Unsaturated Carbonyl Compounds, Phenols and Anilines.

Reactions with Acyclic Terminal Alkenes.

Reaction of simple alkenes with iodonium nitrate gave products of the type shown in equation (1). However, only in the case of 1-hexene were the adducts predicted from considerations of carbonium ion stability (i.e. corresponding to Markovnikov addition), the products being 1-iodo-2-hexyl nitrate 20 (41%) and N(1-iodo-2-hexyl)pyridinium nitrate 21 (42%). The structures of this and other iodonitrate esters were confirmed by zinc-copper couple reduction followed by treatment of the resulting iodohydrin with lithium aluminum hydride (equation 2).

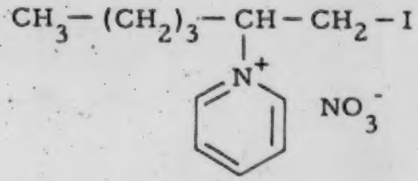
[1]





$$CH_3-(CH_2)_3-\underset{\substack{|\\ ONO_2}}{CH}-CH_2-I$$

20



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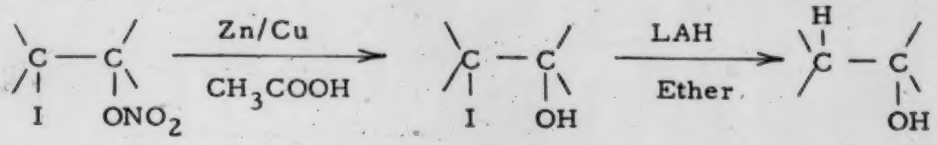
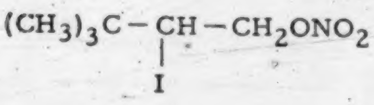
[2]

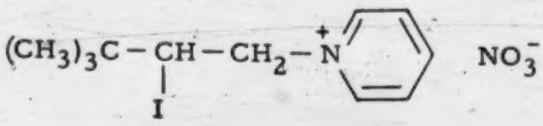


Steric factors appear to play an important role directing the approach of the nitrate ion and pyridine to the initially formed iodonium ion in the case of 3,4-dimethyl-1-hexene and 3,3-dimethyl-1-butene, the former giving a mixture of 70% Markovnikov and 30% anti-Markovnikov addition products. In the case of 3,3-dimethyl-1-butene steric hindrance by the *tert.*-butyl group to the approach of the nucleophile is the overriding factor, the products being the iodonitrate ester **22** (26%) and the pyridinium salt **23** (49%) with the nitrate group



$(CH_3)_3C-\underset{I}{CH}-CH_2ONO_2$

22



23.

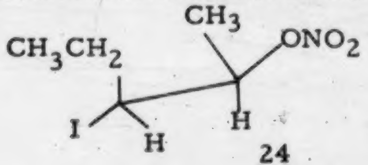
and pyridine respectively at the primary position, as clearly demonstrated by the n.m.r. spectra.

In the assignment of structures to these and similar products by n.m.r. spectrsocopy, it was observed that methine protons alpha to an ONO_2 group absorb in the range 4.8-5.4 δ, whereas methine protons alpha to an iodo function absorb in the range 4.0-5.0 δ[140]. Fowler *et al.* have shown that methylene protons alpha to an iodo function absorb at 3.0-3.5 δ[1]. In the work described here, methylene hydrogens alpha to an iodo group absorbed close to 3.5 δ. For example, the n.m.r. spectrum of 1-iodo-2-hexyl nitrate showed $\delta_{(CDCl_3)}$: 0.7-1.2 (m, 9H, CH_3, 3-CH_2-), 3.35 (d, 2H, -CH_2I), and 4.9 (m, 1H, $-\underline{CH}-ONO_2$). The methylene protons alpha to a nitrate group absorb at around 4.8-5.0 δ and those alpha to a pyridine at around 5.0 δ. The presence of apyridine ring on the α-carbon has a profound influence on the iodomethine hydrogen absorption. The hydrogen is so deshielded that usually the absorptions overlap. Thus the n.m.r. spectrum of **22** showed absorptions at $\delta_{(CDCl_3)}$: 1.15 (s, 9H, -$C(CH_3)_3$), 4.17 (m, 1H, -CH-I), 4.8 (m, 2H, -CH_2-ONO_2) and that of **23** showed

δ_{TMS} [$(CD_3)_2SO$]: 1.22 (1s, 9H, $-C(CH_3)_3$), 4.8-5.3 (m, 3H, -CH-I, $-CH_2-\overset{+}{N}\lessgtr$), 8.1-9.3 (m, 5H, pyridine hydrogens).

Reactions with Acyclic Non-terminal Alkenes.

(Z)-2-Pentene afforded a mixture of 3-iodo-2-pentyl and 2-iodo-3-pentyl nitrates 24 and 25 in a ratio of 70:30 as shown by the n.m.r. spectrum corresponding to a preferential attack by the nitrate ion at the less hindered carbon of the iodonium ion intermediate. It also gave the corresponding iodopyridinium salts 26 and 27 in approximately the same ratio. (For structural proof of the above iodopyridinium nitrates and for more additions to (Z) and (E) pairs of olefins, see Chapter IV). The assignments in the n.m.r. spectra were made on the basis of the empirical chemical shift observations mentioned earlier.



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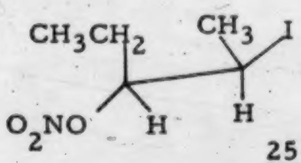

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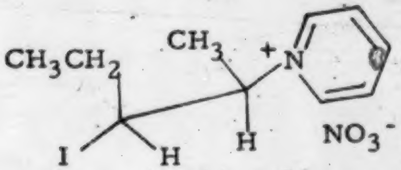

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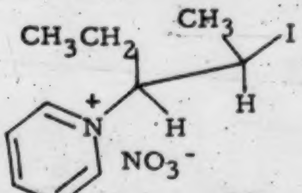

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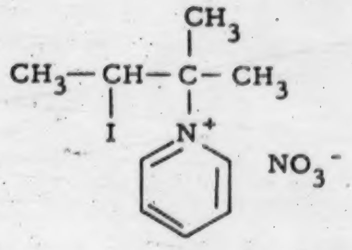
Addition of iodonium nitrate in chloroform-pyridine to olefins in which at least one of the olefinic carbon is disubstituted, provides the iodopyridinium salts often to the complete exclusion of other isolable products. Thus 2-methyl-2-butene gave N[2-(2-methyl-3-iodo)butyl]pyridinium nitrate 28 in 75% yield and 2,3-dimethyl-2-butene gave the analogous iodopyridinium nitrate 29 in 47% yield. The chemical shifts of methyl groups alpha to the pyridinium and iodine groups are very similar. In the case of 29, for example, the starting olefin presented sharp signal in the n.m.r. spectrum at δ1.6.



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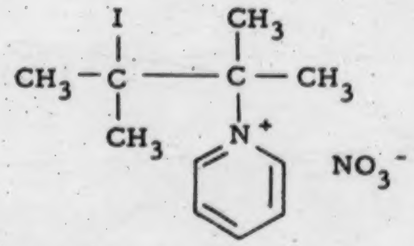
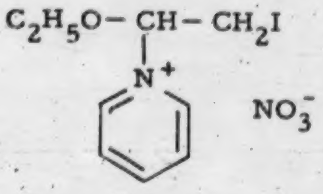


29

The iodopyridinium nitrate 29 on the other hand showed two sharp signals at δ2.08 and 2.05.

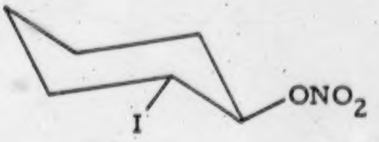
In the case of ethyl vinyl ether, another example in which the carbonium ion involved is considerably stabilized, the pyridine competes successfully with the nitrate ion for the iodonium ion giving N-[1-(1-ethoxy-2-iodo)ethyl]pyridinium nitrate 30 as the exclusive product.



30

Reactions with Cyclic Monounsaturated Compounds.

Addition of iodonium nitrate to cyclic olefins allows a preliminary examination of the stereochemistry of the reaction, which was however more conveniently studied with acyclic olefins (vide infra). Cyclohexene gave two products. The iodoalkyl nitrate 31, obtained in 60% yield, showed the following significant absorptions in the n.m.r. spectrum. δ_{TMS} ($CDCl_3$): 4.17 (m, 1H, -CH-I, $J_{1,2}$=10 Hz, $J_{2,3a}$= 9 Hz, $J_{2,3e}$=5 Hz), 5.15 (m, 1H, $-CH-ONO_2$, $J_{1,2}$=10 Hz, $J_{1,6a}$= 9 Hz, $J_{1,6e}$=5 Hz), which shows a trans stereospecific addition leading to a trans diequatorial conformation 31. Closely related electrophilic additions to alkenes have been demonstrated to be *trans* stereospecific[1,141]. This conformation was insensitive to changes in the polarity of the solvent ($CDCl_3$, CCl_4, C_6H_6, CD_3CN). In this



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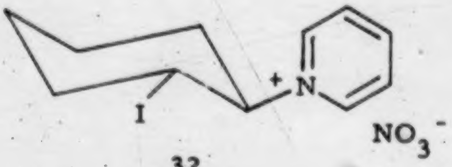
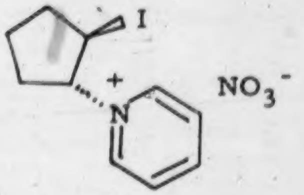


32

reaction the corresponding iodopyridinium nitrate 32 was obtained in 40% yield, the n.m.r. spectrum of which showed $\delta_{TMS}[(CD_3)_2SO]$:4.9 (m, 2H, -CH-I, -CH-$\overset{+}{N}{<}$), 2.5 (m, 2H, -$\underline{CH}_2$CH-I, -$\underline{CH}_2$-CH-$\overset{+}{N}{<}$), 2.1 (m, 4H, 2-CH_2-). The signals corresponding to the pyridinium ring appeared at δ 8.35, 8.8 and 9.35 as three multiplets integrating in the ratio of 2:1:2.

The reaction of cyclopentene with iodonium nitrate gave 2-iodocyclopentyl nitrate 33 in 53% yield and N-(2-iodocyclopentyl)-pyridinium nitrate 34 in 9% yield. Cycloheptene and cyclooctene



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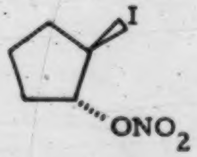

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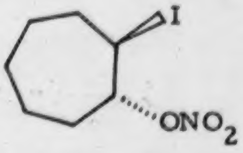
reacted similarly. Cycloheptene produced 2-iodocycloheptyl nitrate 35 in 68% yield and the corresponding iodopyridinium nitrate 36 in



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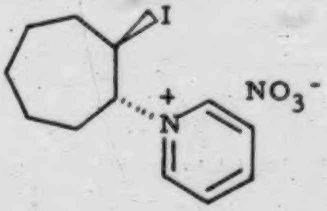
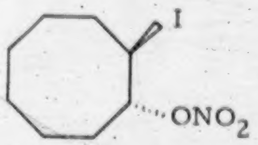


36

11.5% yield. Cyclooctene afforded 2-iodocyclooctyl nitrate 37 in 79% yield and N-(2-iodocyclooctyl)pyridinium nitrate 38 in 5.5% yield.



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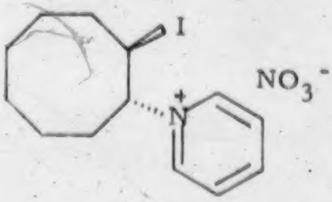
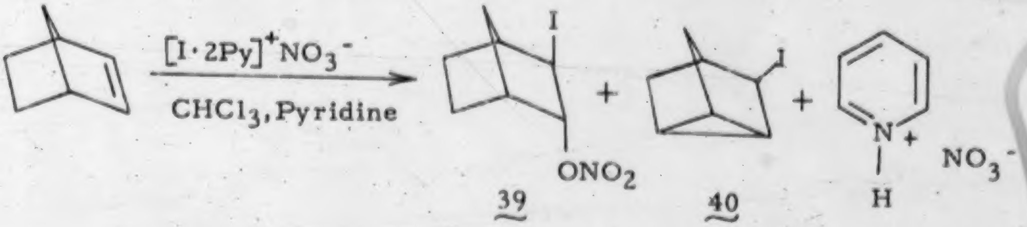


38

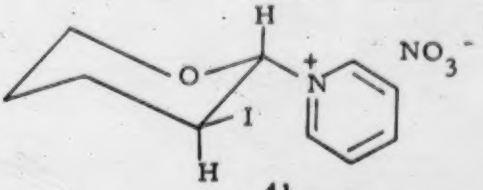
In the above three cases, it is to be noted that the yield of the iodopyridinium nitrates is considerably less than in the case of cyclohexene. This may be attributed to the increased steric hindrance for the approach of the nucleophilic pyridine to the intermediate iodonium ion.

Norbornene on reaction with iodonium nitrate gave the expected iodonitrate ester 39 in approximately 60% yield. However no iodopyridinium salt was produced. Instead, the nortricyclanyl iodide 40 was formed in 40% yield together with a corresponding amount of pyridinium nitrate.



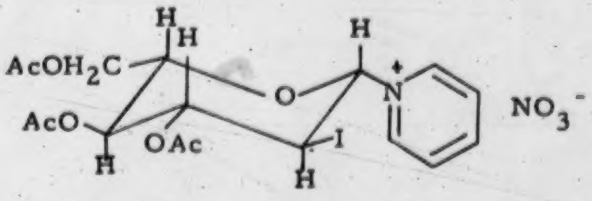
39 40

Addition of iodonium nitrate to 2,3-dihydropyran produced trans equatorial N-(3-iodo-tetrahydropyranosyl)pyridinium nitrate 41,

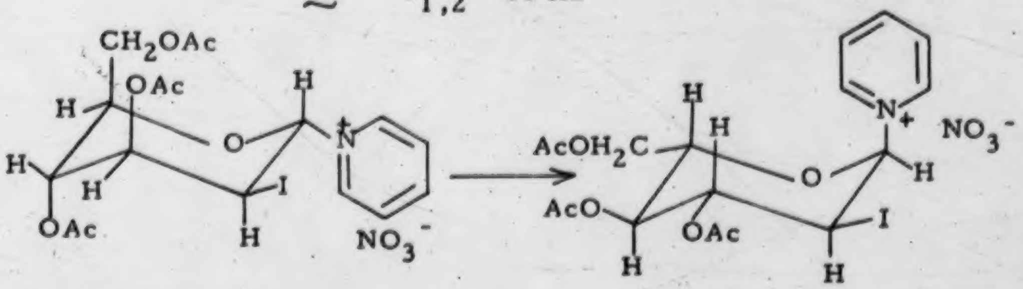


41

the n.m.r. spectrum of which (anomeric proton) δ in $(CD_3)_2SO$, 6.38 (d, 1H, $J_{1,2}$=10 Hz) closely resembles that of similar substances reported by Lemieux and Morgan[142]. Similarly reaction D-glucal triacetate with iodonium nitrate gave only iodopyridinium salts. One product, formed in 27% was shown to be the all-*trans* isomer 42 on the basis of the n.m.r. spectrum. The anomeric proton absorbed at $\delta_{TMS}[(CD_3)_2SO]$: 6.73 (d, 1H, $J_{1,2}$=10 Hz). All other ring protons had coupling constants close to 10 Hz. The remaining material, obtained as an oil in 29% yield, was purified by chromatography on florisil. The n.m.r. spectrum showed the presence of two isomers, assigned structures 43 and 44. The major isomer 43 had the anomeric proton absorption at $\delta_{TMS}[(CD_3)_2SO]$: 6.71 (d, $J_{1,2}$=10 Hz) and was different from the all-*trans* isomer 42. On allowing to stand in dimethyl sulfoxide, the proportion of 44 was found to increase. 44 had its anomeric proton absorption at δ 6.56 ($J_{1,2}$=6 Hz). Crystallization of the oil from ethanol gave the all-*trans* isomer 42.



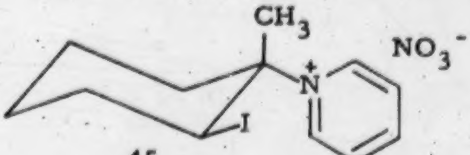
42 $J_{1,2}$ = 10 Hz



43 $J_{1,2}$= 10 Hz

44 $J_{1,2}$= 6 Hz

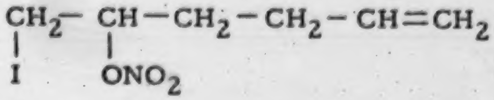
In contrast to the case of cyclohexene, the corresponding iodonitrate ester could not be isolated, in keeping with the finding that compounds which give rise to very stable carbonium ion intermediates react preferentially to give the iodo-pyridinium salts. This is demonstrated by contrasting the reaction of cyclohexene (vide supra) with that of 1-methylcyclohexene in which the only isolable product was the N-[1-(1-methyl-2-iodocyclohexyl)] pyridinium nitrate 45 in 25% yield.



45

Reactions with Unconjugated Dienes.

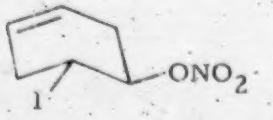
Upon reaction of an unconjugated diene with one equivalent of iodonium nitrate, only one double bond reacted giving the iodoalkene nitrate ester and/or the iodoalkene pyridinium nitrate depending on the degree of substitution in the substrate. For example 1,5-hexadiene gave a 1:1 adduct with the characteristic n.m.r. absorption for the $-CH_2I$ and $-CH-ONO_2$ groups. $\delta_{TMS}(CDCl_3)$: 2.0 (m, 4H, 2 $-CH_2-$), 3.35 (d, 2H, $-CH_2I$), 5.13 (m, 3H, $=CH_2$ and $-CH-ONO_2$) and 5.6 (m, 1H, $=CH-$). Accordingly structure 46 was assigned to this product, corresponding to Markovnikov addition. 1,4-Cyclohexadiene behaved



$$\underset{\displaystyle I}{\underset{|}{CH_2}}-\underset{\displaystyle ONO_2}{\underset{|}{CH}}-CH_2-CH_2-CH=CH_2$$

46

in a similar way to other unconjugated alkenes and gave 5-iodocyclohexenyl nitrate 47 in 27% yield and N-[4-(5-iodocyclohexenyl)]-pyridinium nitrate 48 in 24% yield.



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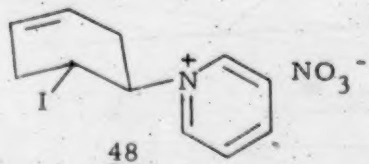
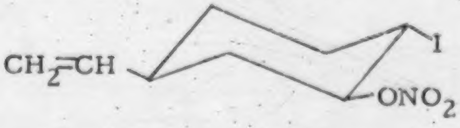


48

The reaction of 4-vinylcyclohexene with iodonium nitrate allows an examination of competition in the electrophilic addition to acyclic and cyclic alkenes within the same model. The products proved to be the iodonitrate ester 49 in 25% yield and the iodopyridinium salt 50 in 27% yield corresponding to addition exclusively in the ring. The alternative structure for 49 in which addition takes place to the



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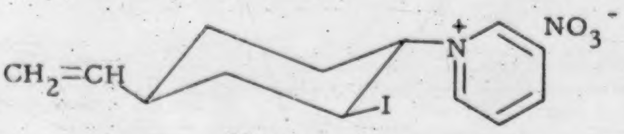
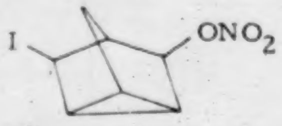


50

vinyl group may be immediately excluded because of the absence in 3.5-3.0 δ region of the n.m.r. spectrum of a signal characteristic of $-CH_2-I$. On similar grounds the comparable alternative structure for 50 may also be excluded. The positions of the iodine and nitrate groups in 49 and the iodine and pyridinium groups in 50 on the 1,2-cyclohexane bond can not be assigned unambiguously. The marked preference for electrophilic additions in this case to the cyclic olefinic bond may be ascribed to the greater stability of the resulting iodonium ion.

Norbornadiene on reaction with iodonium nitrate gave two products corresponding to cross-ring interaction, i.e., tricyclo-$[2\cdot 2\cdot 1\cdot 0^{2,6}]$-5-iodohept-3-yl nitrate 51 in 64% yield and the corresponding iodopyridinium salt 52, N-[3-(5-iodonortricyclanyl)]pyridinium nitrate, in 10% yield. The n.m.r. spectrum of 51 showed no olefinic protons and was consistent with a tricyclane structure.



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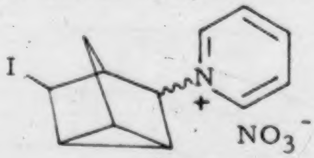

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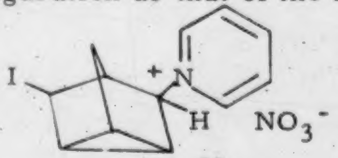
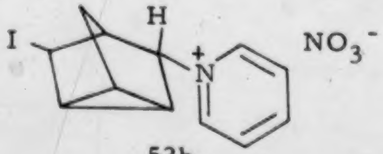
Examination of the n.m.r. spectrum of 52 showed it to consist of a mixture of two isomers 52a and 52b, the former having the same configuration as that of the major product 51. The above reaction



52a



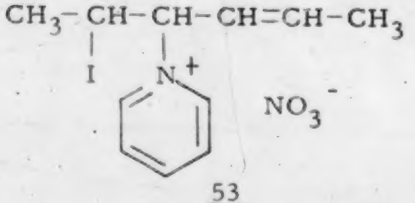
52b

resembles the addition of iodine isocyanate to 5-methylenenorbornene reported by Hassner and co-workers[96] and also resembles products obtained by Grimwood and Swern[101].

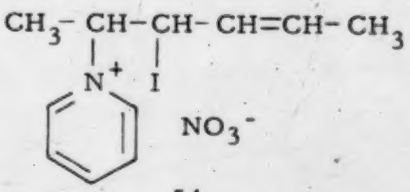
Reactions with Conjugated Dienes.

In all the examples studied of addition to conjugated dienes only the iodopyridinium salts were obtained and they corresponded exclusively to 1,2-addition of one equivalent of iodonium nitrate except in one case (vide infra). In these cases the carbonium ion involved is allylic and the sole formation of the pyridinium salt is consistent with the observation that this is the major type of product obtained when a stable carbonium ion is involved as in the case of monoolefins discussed above.

Reaction of 2,4-hexadiene produced N-[4-(5-iodo-2-hexenyl)]pyridinium nitrate 53 in 70% yield. The possibility of a 1,4-addition was discounted since the n.m.r. spectrum showed two well separated doublets at δ 2.0 and 1.75 with J=7 and 5 Hz respectively, corresponding to two methyl groups in quite different



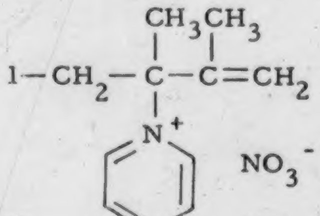
53



54

environments whereas other model compounds show that methyl groups alpha to an iodo group have similar chemical shifts to those of methyl groups alpha to a pyridinium group. The n.m.r. spectrum is consistent with either the Markovnikov structure 53 or the anti-Markovnikov structure 54. However structure 53 is preferred from mechanistic considerations since the pyridine would be expected to attack the more stable allylic cationic centre.

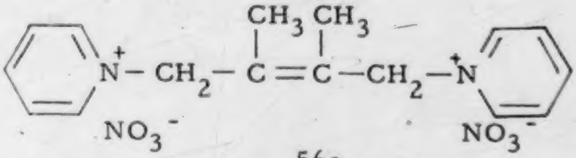
2,3-Dimethyl-1,3-butadiene was the only conjugated diene which gave an adduct corresponding to 1,4-addition. With iodonium nitrate it afforded N-[3-(4-iodo-2,3-dimethyl)but-1-enyl]pyridinium nitrate 55 corresponding to 1,2-addition in 60% yield and another product (5.5% yield), to which structure 56 is assigned on the basis of the n.m.r. spectrum and elemental analysis. The n.m.r. spectrum



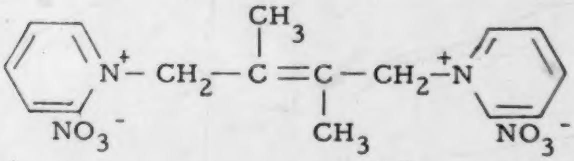
55

of 55 was consistent with a 1,2-addition because it showed a pattern characteristic of the terminal vinylic protons. Again the two methyl groups were in quite different environments.

Inspection of the n.m.r. spectrum of 56 shows it to be highly symmetrical. δ_{D_2O}: 1.82 (s, 6H), 5.4 (s, 4H). Examination of the integration of the pyridine protons reveals that the molecule contains two pyridine groups. Since the n.m.r. spectrum is consistent with either structure 56a or 56b it is difficult at this point to assign any particular structure to the compound.



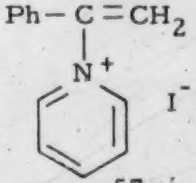
56a



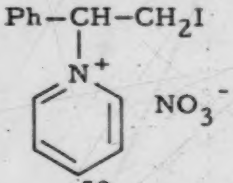
56b

Product 56 may be envisaged as arising from 1,4-addition followed by displacent of the allylic iodine by pyridine as outlined in Scheme 4. Addition of bromonium nitrate to 2,3-dimethyl-1,3-butadiene (*vide infra*) and the fact that no equilibration of benzylic centres is observed in the addition of iodonium nitrate to aryl substituted olefins (see Chapter IV) argue against this pathway for the formation of compound 56.

Reaction of styrene with iodonium nitrate gave three products. N-[1-(1-Phenylethenyl)]pyridinium iodide 57 and N-[1-(phenyl-2-iodo)-ethyl]pyridinium nitrate 58 were formed in a combined yield of 75-80% as indicated by the n.m.r. spectrum of the crude pyridinium salts.

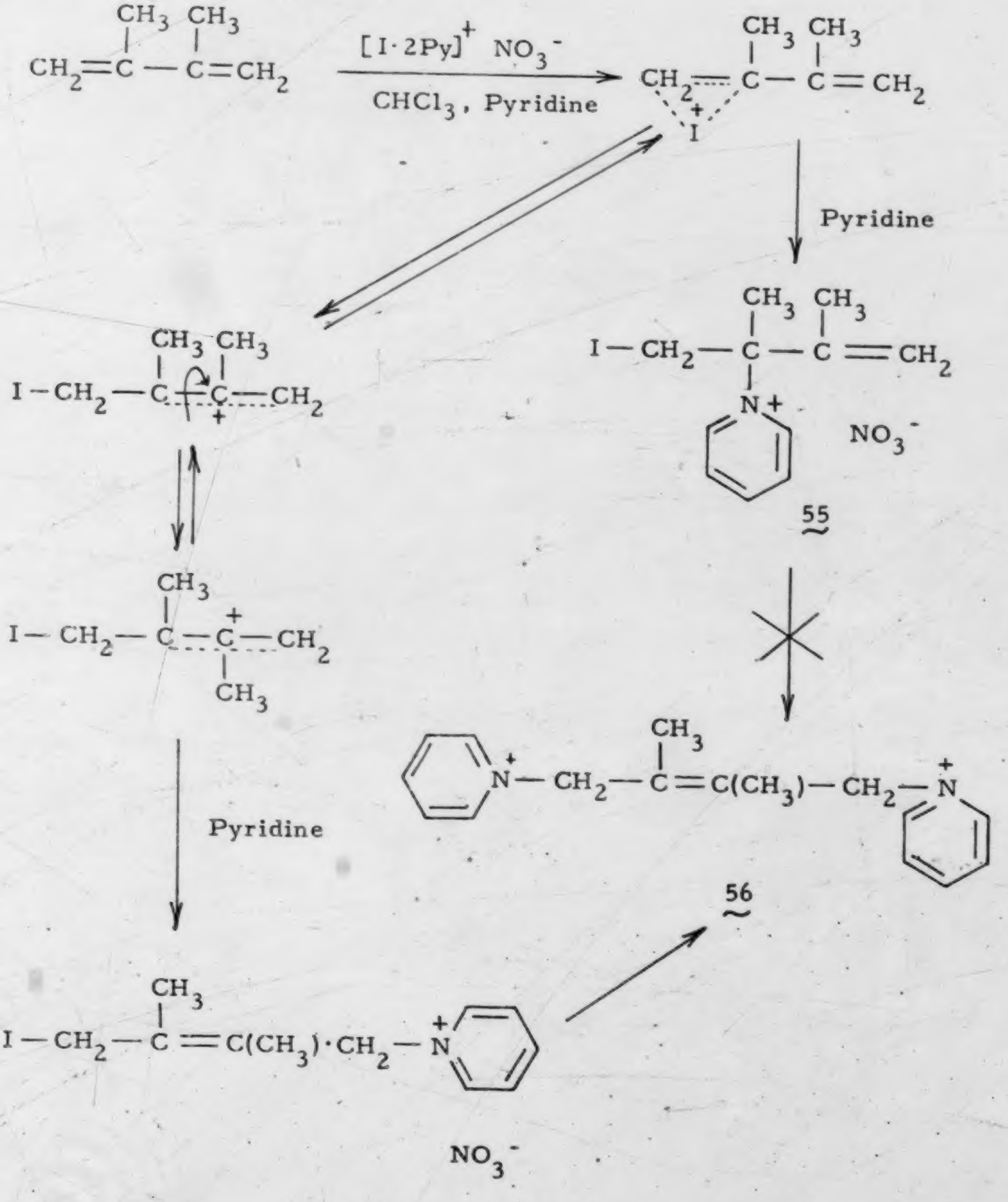


57



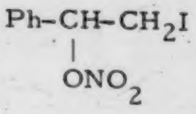
58

They were not separable by the usual methods. 58 could be converted to 57 by treatment with potassium carbonate in water. Approximately 10% yield of the iodonitrate ester 59 was



[I·2Py]$^+$ NO$_3^-$
CHCl$_3$, Pyridine
Pyridine
55
56
Pyridine
NO$_3^-$
NO$_3^-$

Scheme 4

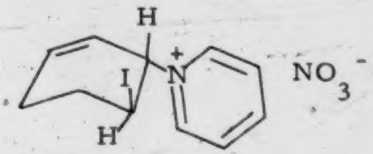


$$\begin{array}{l}Ph\text{-}CH\text{-}CH_2I\\ \quad\quad |\\ \quad\quad ONO_2\end{array}$$

59

also isolated. This product could not be purified because it suffers extensive decomposition when distilled. However n.m.r. and mass spectrometry evidence was consistent with the assigned structure.

An example of iodonium nitrate addition to a cyclic conjugated diene is provided by 1,3-cyclohexadiene which gave the pyridinium salt 60 in 60% yield.

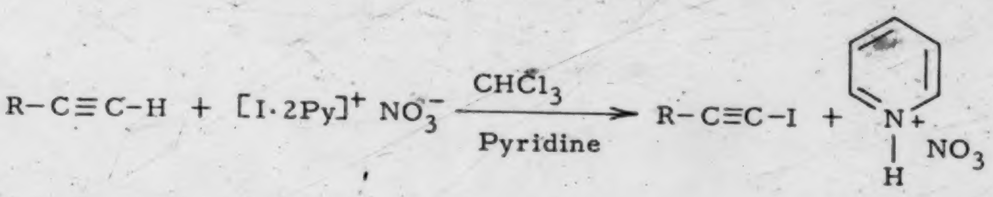


60

Reactions with Acetylenic Compounds.

Non-terminal acetylenes were unreactive towards electrophilic addition of iodonium nitrate. However terminal acetylenes reacted readily to give alkynyl iodides according to equation 3. Pyridinium nitrate was obtained in stoichiometric quantity indicating complete replacement of the acidic proton of the acetylene. Some

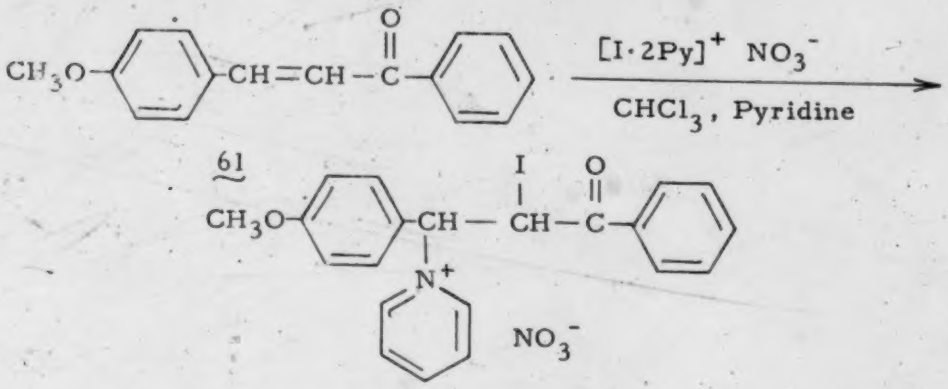
[3]



tar formation took place with a consequent decrease in yield of product. The structure of the iodoacetylenes were fully consistent with the analytical and spectra data. The terminal iodocompounds produced in this was are summarised in Table 1.

Reactions with α,β-Unsaturated Carbonyl Compounds

Iodonium nitrate was unreactive towards α,β-unsaturated ketones and esters. Thus no addition product could be isolated when methyl trans-crotonate was exposed to iodonium nitrate for 24 h. Similarly chalcone was recovered unchanged on treatment with iodonium nitrate. On the other hand para-methoxychalcone 61 did react to afford the iodopyridinium nitrate 62 as the sole product in 91% yield. The assignment of the regiochemistry for 62 is based on the fact that



61

62

the nucleophilic attack of pyridine would be favored at the more stable cationic centre of the iodonium ion intermediate. In this case the para-methoxy group effectively increases the electron density at the double bond, compared to the parent chalcone, enabling it to react with iodonium nitrate.

Reactions with Phenols and Anilines.

As part of our investigation on neighboring group participation (vide infra) in the addition of iodonium nitrate to suitable olefinic substrates, we carried out the reaction of 2-allylphenols with this

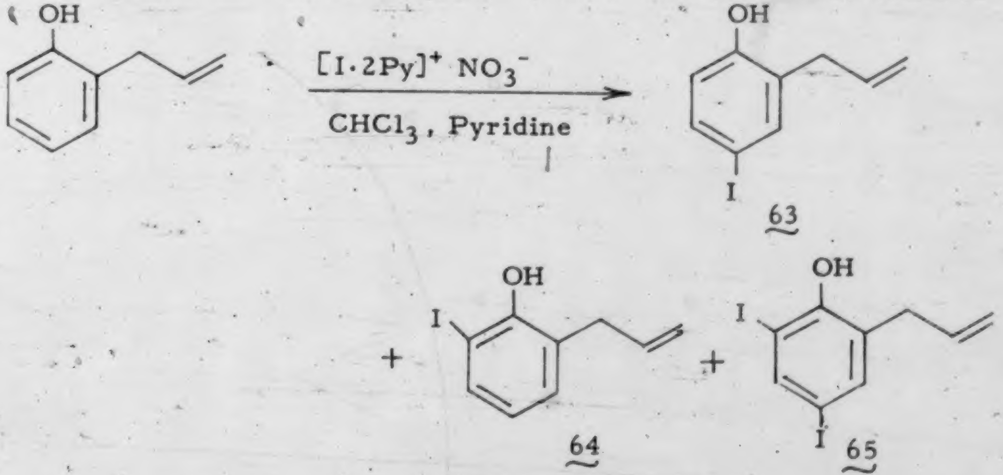
Table-1

Iodoacetylene Compounds.

1-Alkyne	Alkynyl iodide				
	Yield (%)	b.p. (^{o}C/mm)	lit. b.p. (^{o}C/mm)	Molecular ion	Reference
1-Octyne	40*	58/0.7	95-97/7.5	236	143
Phenylacetylene	60	73/0.7		228	144
Methylacetylene	45	100/700	110/760	166	143, 145

* Anal. Calcd. for $C_8H_{13}I$: C, 40.70; H, 5.55. Found: C, 41.10; H, 5.54.

reagent. Reaction of 2-allylphenol with one molar equivalent of iodonium nitrate did not give the expected double bond addition product, but instead gave the aromatic iodination products 63-65 along with the corresponding amount of pyridinium nitrate. The iodine was found to



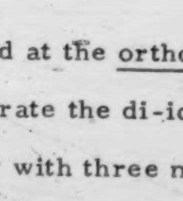
63

64

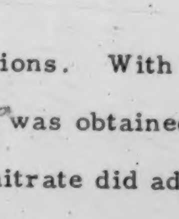
65

be introduced at the ortho and/or para positions. With two moles of iodonium nitrate the di-iodinated product 65 was obtained in 74.5% yield. Only with three moles of iodonium nitrate did addition to the double bond occur, with the addition proceeding only after all the available ortho and para positions are iodinated. We decided to investigate the scope of this reaction for the iodination of activated aromatic molecules.

Phenol reacted with three molar equivalents of iodonium nitrate to give 2,4,6-triiodophenol 66 in 94% yield. Similarly para-cresol afforded a 90% yield of 2,6-diiodo-4-methylphenol 67 with two moles of iodonium nitrate.

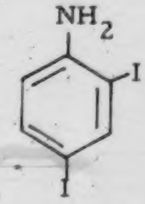


66



67

Aromatic primary amines reacted with iodonium nitrate to give the corresponding iodinated products in low yields. In these cases it was observed that a considerable amount of tar is produced, probably by oxidation of the amino group. It was also observed that a maximum of two iodine atoms can be introduced. Thus aniline with excess (3 moles) of iodonium nitrate gave 2,4-di-iodoaniline 68 in 46% yield and *para*-toluidine gave the corresponding diiodo compound 69 in 23% yield.



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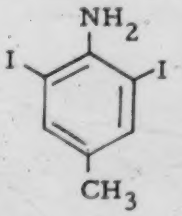
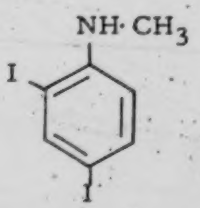
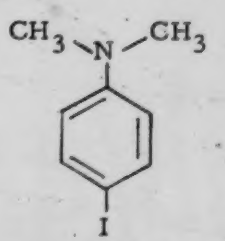


69

The reaction of aromatic secondary and tertiary amines was cleaner in that the iodinated products were obtained in good to excellent yields. Thus N-methylaniline with excess of iodonium nitrate gave a 78% yield of 2,4-diiodo-N-methyl-aniline 70. In the case of N,N-dimethylaniline, the reaction was regiospecific in that only the *para*-iodinated product 71 was formed in 94.5% yield.



70



71

In contrast to other electrophilic aromatic substitution reactions, the presence of a methoxy group is not sufficient for such compounds to react with iodonium nitrate. Thus *para*-methylanisole did not react with iodonium nitrate even after several days.

As mentioned earlier only two of the three available *ortho* and *para* positions in aromatic primary and secondary amines could be substituted with iodonium nitrate, in contrast to phenol. This may be due to the deactivation of the ring as a result of the introduction of the two iodine atoms. Steric factors may play a role (cf. aniline and N-methylaniline) because in aniline the two iodine atoms introduced are at *ortho* and *para* positions, not at the two *ortho* positions.

The characteristics of the reactions so far discussed are summarized in Table-2.

Table 2

Characteristics of the Reaction of Iodonium Nitrate with Various Substrate-types

Substrate-type	Reaction-type	Products	Regiochemistry	
			Esters	Pyridinium salts
Terminal olefins	Addition	Ester, pyridinium salt	Markovnikov from C_6 onwards.	Markovnikov from C_6 onwards
Nonterminal disubstituted acyclic olefins	Addition	Ester, pyridinium salt	Anti-Markovnikov preferred	Anti-Markovnikov preferred
Unsubstituted cyclic olefins	Addition	Ester, pyridinium salt	-	-
Trisubstituted and tetrasubstituted acyclic olefins, substituted cyclic olefins and vinyl ethers	Addition	Pyridinium salt	-	Markovnikov
Mono aryl substituted olefins	Addition	Ester, pyridinium salt, vinyl pyridinium salt	Markovnikov	Markovnikov
Unconjugated dienes	Addition	Ester, pyridinium salt	Markovnikov	Markovnikov
Conjugated dienes	Addition	Pyridinium salt	-	Markovnikov, 1,2-addition
Bicyclic mono olefins	Addition Hydride transfer	Ester	-	-

. . . Continued

Table 2 - Continued

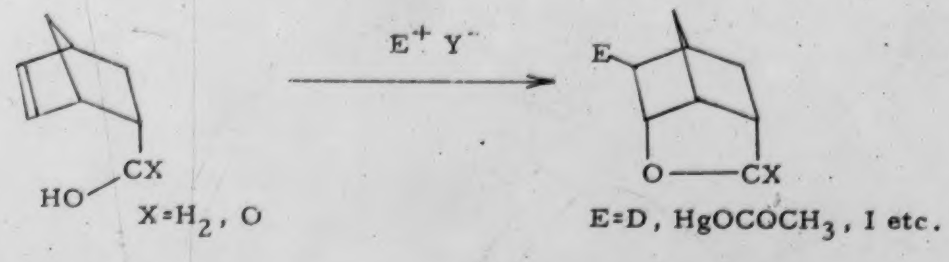
Substrate-type	Reaction-type	Products	Regiochemistry	
			Esters	Pyridinium salts
Bicyclic dienes	Rearrangement	Ester , pyridinium salt	-	-
Nonterminal acetylenes	No reaction	-	-	-
Terminal acetylenes	Substitution	-	-	-
α,β-Unsaturated carbonyl compounds	No reaction*	-	-	-
Phenols and anilines	Aromatic substitution	ortho, para-Iodophenols and iodoanilines	-	-

*Exception: para-methoxychalcone

CHAPTER III

Addition of Iodonium Nitrate to Olefinic Alcohols and Allylphenols — Neighboring Group Participation.

Neighboring group participation has been observed for a variety of groups in many types of reaction[146], evidence for which comes from abnormally high reaction rates and from the formation of cyclic or rearranged products. Most of the work has involved aliphatic nucleophilic substitutions where the neighboring group acts as an intramolecular nucleophile. Similar type of behaviour is to be expected in electrophilic addition reactions although the intermediates are not necessarily carbonium ions but may be bridged ions (e.g. halonium ions). This has been found to be true in the addition of bromine and iodine to olefinic alcohols of the type $CH_2=CH-(CH_2)_n-OH$, where cyclic ethers have been isolated for n=3 and 4[137,147]. Cyclized products are also formed in other electrophilic addition reactions[148].



Participation and subsequent migration of phenyl group have been observed in the addition of bromine[149], iodine mono-chloride, iodine isocyanate, iodine azide[106] and bromine azide[107] to triphenylpropene. On the other hand no participation by hydroxy group occurs in the addition of iodine isocyanate to 1,1-dimethylallyl alcohol.

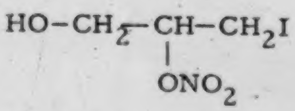
The iodonium nitrate reagent readily dehydrogenates primary and secondary aliphatic alcohols and benzyl alcohols to the corresponding carbonyl compounds. In this reaction[150] the order of reactivities of these alcohols is benzylic $\rangle$ secondary $\rangle$ primary.

Since allylic alcohols have the same redox potentials as benzyl alcohol[151] and these potentials are lower than those for saturated primary alcohols, it was anticipated that allylic alcohols should be more readily dehydrogenated by iodonium nitrate. So the purpose of this investigation was to examine the competition between electrophilic addition and dehydrogenation reactions and to explore possibilities for neighboring group participation in suitable unsaturated systems.

In all the cases studied, electrophilic addition proved to be the dominant type of reaction. Even in the case when a 1 mole excess of reagent was used no oxidation to a carbonyl compound was observed. Also in the case of certain alcohols, hydroxy group participation resulted in the formation of three, four and five membered cyclic ethers. The reactions were carried out both in chloroform-pyridine and chloroform-sym-collidine. In the former solvent iodopyridinium nitrates were formed together with products of direct electrophilic addition. Use of sym-collidine which is non-nucleophilic prevented formation of the iodo-quaternary salts and allowed isolation and examination of the other reactions.

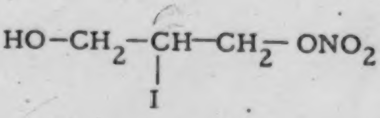
Reactions with Allylic Alcohols.

Allyl alcohol on reaction with iodonium nitrate in chloroform-pyridine formed an isomeric mixture (ratio 80:20) of iodonitrates **72** and **73** in 30% yield. The composition of the mixture in this and similar



$\mathrm{HO{-}CH_2{-}\underset{\displaystyle ONO_2}{\underset{|}{CH}}{-}CH_2I}$

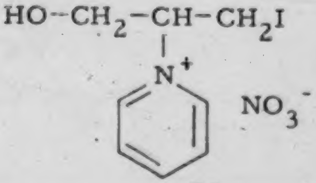
72



$\mathrm{HO{-}CH_2{-}\underset{\displaystyle I}{\underset{|}{CH}}{-}CH_2{-}ONO_2}$

73

cases was determined by measuring the ratio of the intensity of the $-CH_2I$ n.m.r. absorption to that of the rest of the spectrum. The corresponding iodo-pyridinium salt consisted of two isomers 74 and 75 in a ratio of 75:25 which were formed in a combined yield of 23%.



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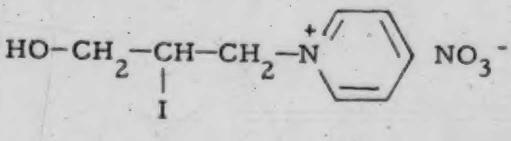
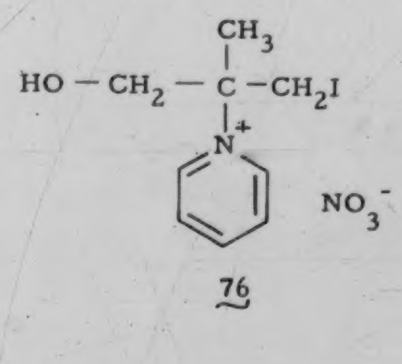


75

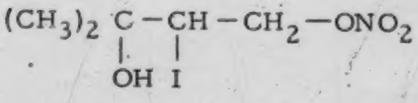
Reaction of iodonium nitrate with allyl alcohol when performed in chloroform-*sym*-collidine increased the yield of the iodo-nitrates to 60% and no quaternary salt was formed.

Substitution of the central carbon atom of the allylic system with a methyl group results in the increased stabilization of the corresponding carbonium ion which is reflected in the formation of the iodo-pyridinium salt 76 to the complete exclusion of other isolable products in the case of 2-methylallyl alcohol.



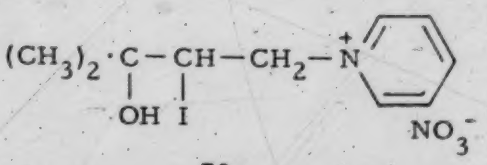
76

The reaction of 1,1-dimethylallyl alcohol with iodonium nitrate in chloroform-pyridine produced one isomeric form of the iodonitrate 77 in 20% yield and only one iodopyridinium salt 78 in 40% yield corresponding to anti-Markovnikov-type addition. That this



$$\begin{array}{l}(CH_3)_2\,\underset{\displaystyle OH}{\underset{|}{C}}-\underset{\displaystyle I}{\underset{|}{C}H}-CH_2-ONO_2\end{array}$$

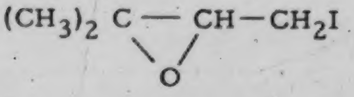
77



78

effect may be attributed to steric hindrance by the three groups at the 1-position of the allyl alcohol is demonstrated by the exclusive formation of anti-Marknovnikov addition products from the reaction of iodonium nitrate with 3,3-dimethylbut-1-ene (*vide supra*). Precisely the same mode of addition has been observed in the reaction of 1,1-dimethylallyl alcohol with iodine isocyanate[96].

In contrast to the reaction of 1,1-dimethylallyl alcohol in chloroform-pyridine, its reaction with iodonium nitrate in chloroform-*sym*-collidine takes a different course, the products being the iodonitrate 77 and the epoxide 79. The epoxide structure 79 was proven



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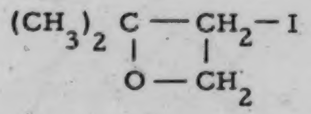
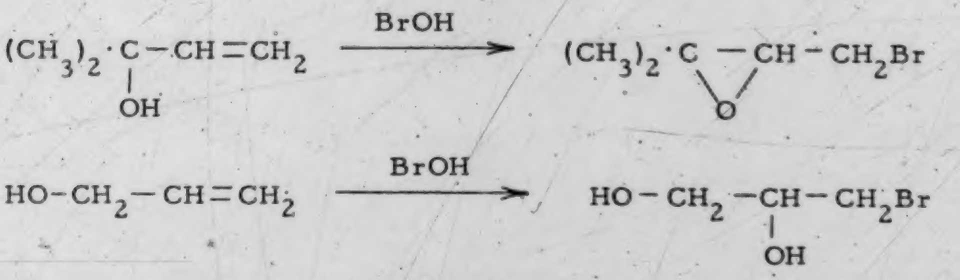


80

and the alternative oxetan structure 80 discounted by the ready reductive cleavage with lithium aluminum hydride in ether at 5° to *tert.*-pentyl alcohol, identified by comparison with an authentic sample. Oxetans require much more vigorous conditions for reductive cleavage[152]. The isolation of epoxide in this and other cases involving allylic alcohols in which the hydroxy-bearing carbon atom is secondary or tertiary, (in contrast with the behaviour of allyl alcohol) is in agreement with the observation of Winstein and Goodman on the addition of hypobromous acid to allylic alcohols[153,154].



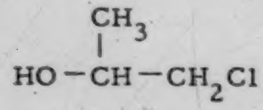
$(CH_3)_2\cdot C(OH)-CH=CH_2$
BrOH
$(CH_3)_2\cdot C$ — CH — CH_2Br
O
$HO-CH_2-CH=CH_2$
BrOH
$HO-CH_2-CH(OH)-CH_2Br$

The facilitating effect of alkyl substitution upon epoxide formation is also illustrated by the following comparison of rate constants[155] (water at 18°):

$k_{rel.}$

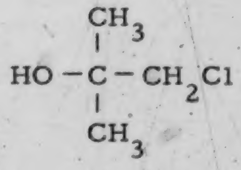
$HO-CH_2-CH_2-Cl$

1.0



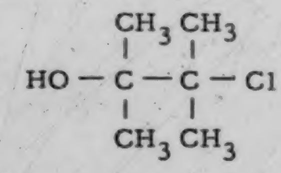
$HO-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_2Cl$

21



$HO-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_2Cl$

250

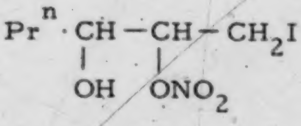


$HO-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-Cl$

1370

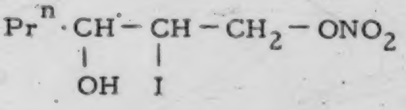
The effect has been attributed to relief of steric crowding in the parent chlorohydrin as the epoxide is formed[156,157].

The lesser steric hindrance offered to approaching nitrate ion by the iodonium ion formed from a secondary allylic alcohol compared with that from a tertiary alcohol is illustrated by hex-1-en-3-ol. In chloroform-pyridine the isomeric mixture of iodonitrates 81 and 82 (50:50) was produced in 34% yield, indicating the less stringent steric demands of the intermediate iodonium ion. However, the greater size



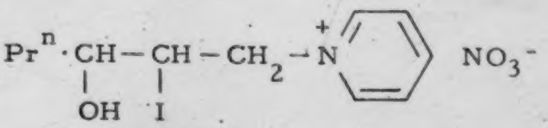
$\mathrm{Pr^n\cdot CH(OH)-CH(ONO_2)-CH_2I}$

81



$\mathrm{Pr^n\cdot CH(OH)-CH(I)-CH_2-ONO_2}$

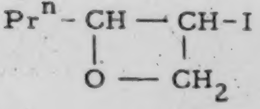
82



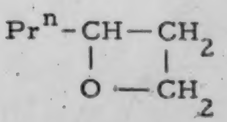
83

of the pyridine results in the exclusive formation of the 2-iodo-1-pyridino-nitrate 83.

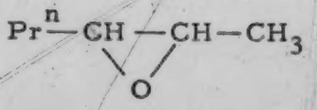
The reaction of hex-1-en-3-ol in chloroform-sym-collidine gave the oxetan 84, which was completely resistant to reductive cleavage by lithium aluminum hydride in ether at 5° for 1.5 h. under conditions in which compound 79 was cleaved in 10 minutes. Treatment of the oxetan with lithium aluminum hydride in tetrahydrofuran



84



85

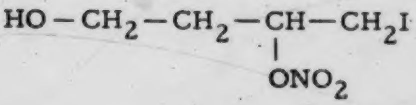


86

for 24 h. at 60° removed it completely. The main product was 2-propyl oxetan 85 and only traces of hexan-3-ol were produced consistent with the known resistance of oxetans to reductive cleavage[152]. The alternative 2,3-epoxyhexane structure 86 would not have survived the reduction process.

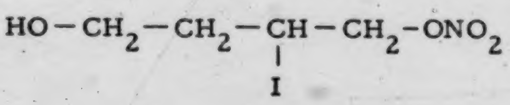
Reactions with Homo-allylic Alcohols.

At this point it was of interest to examine the behaviour of homoallylic alcohols. But-3-en-1-ol on reaction with iodonium nitrate in chloroform-pyridine gave isomeric (85:15) iodonitrates 87 and 88 in 34% yield, as determined by comparison of the n.m.r. intensity of $-CH_2I$ and $-\underline{CH}_2OH$, which absorbed at $\delta_{TMS}(CDCl_3)$: 3.43 (d) and 3.78 (t) respectively. The corresponding pyridinium salt obtained in 54% yield was again



$$HO-CH_2-CH_2-\underset{\underset{ONO_2}{|}}{CH}-CH_2I$$

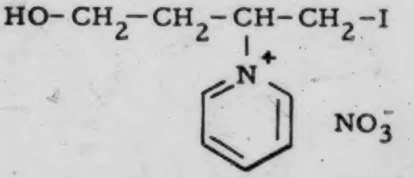
87



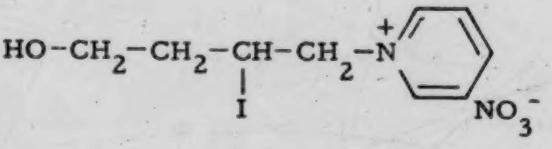
$$HO-CH_2-CH_2-\underset{\underset{I}{|}}{CH}-CH_2-ONO_2$$

88

shown to be a mixture of the Markovnikov product 89 and the anti-Markovnikov product 90 in an approximate ratio of 2:1, as determined



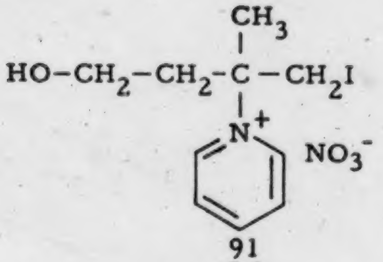
89



90

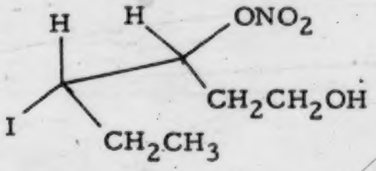
by comparison of the n.m.r. intensities of $-\underline{CH}_2-CHI$ and $-\underline{CH}_2-CH-\overset{+}{N}\lessgtr$, which absorbed as quartets at $\delta_{TMS}[(CD_3)_2SO]$: 1.98 and 2.35. Here the assumption is made that the methylene protons adjacent to a pyridino - methine group will be more deshielded than the corresponding protons adjacent to an iodomethine group.

As in the case of allylic systems, substitution of the central carbon atom of the homoallylic system with a methyl group results in the exclusive formation of the iodopyridinium nitrate as exemplified by the addition of iodonium nitrate to 3-methylbut-3-en-1-ol, which gave 91 in 61% yield.

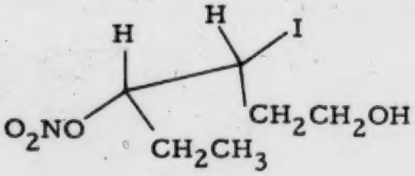


91

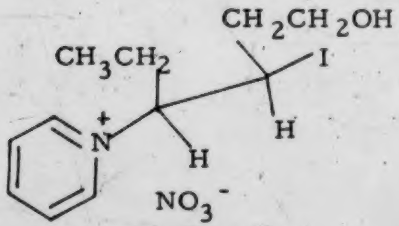
Hex-3-en-1-ol reacted with iodonium nitrate in chloroform-pyridine to give a mixture of iodonitrates 92 and 93 in 62% yield and in a ratio of approximately 1:1. The heterogeneous nature of the iodonitrate fraction was evident from the n.m.r. spectrum which presented four series of multiplets from δ_{TMS} ($CDCl_3$): 4.1 to 5.6, characteristic of two -CH-I and two -CH-ONO_2 groups. No cyclized product could be isolated in this reaction. The iodopyridinium salt formed in 10% yield had a clean n.m.r. spectrum which is consistent with either structure 94 or 95. A conclusion as to whether it is 94 or 95 or a mixture of both could not be made.



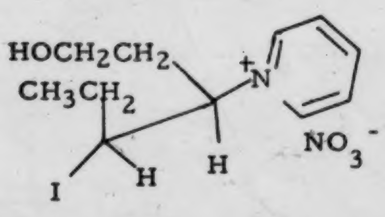
92



93



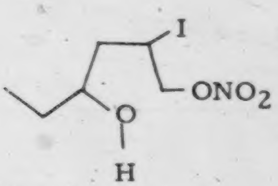
94



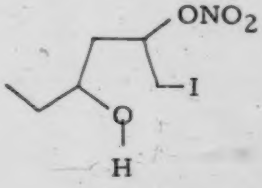
95

Parallel reaction of 2-hex-3-en-1-ol in chloroform-sym-collidine gave the iodonitrates 92 and 93 in approximately the same proportion in 59% yield. No cyclic ether could be isolated in this case either.

The effect of alkyl substitution on hydroxy-bearing carbon atom was examined. In chloroform-pyridine with iodonium nitrate hex-5-en-3-ol gave the isomeric iodonitrates 96 and 97 in a ratio of

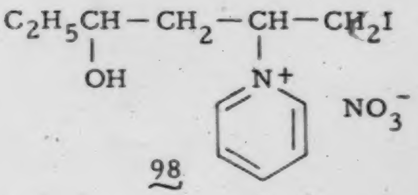


96



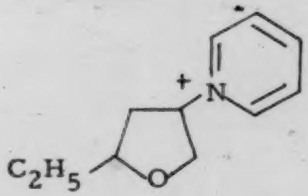
97

25:75. The isolated pyridinium salt was not the expected N-[2-(4-hydroxy-1-iodohexyl)]pyridinium nitrate 98. Instead N-(5-ethyltetrahydrofuran-3-yl)pyridinium nitrate 99 was obtained in 20% yield, as shown by its n.m.r. and i.r. spectra and elemental analysis. In



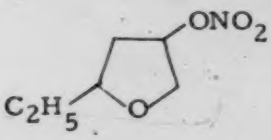
$C_2H_5CH(OH)-CH_2-CH(N^+C_5H_5)-CH_2I \quad NO_3^-$

98



99

chloroform-sym-collidine 5-ethyltetrahydrofuran-3-yl nitrate 100 was

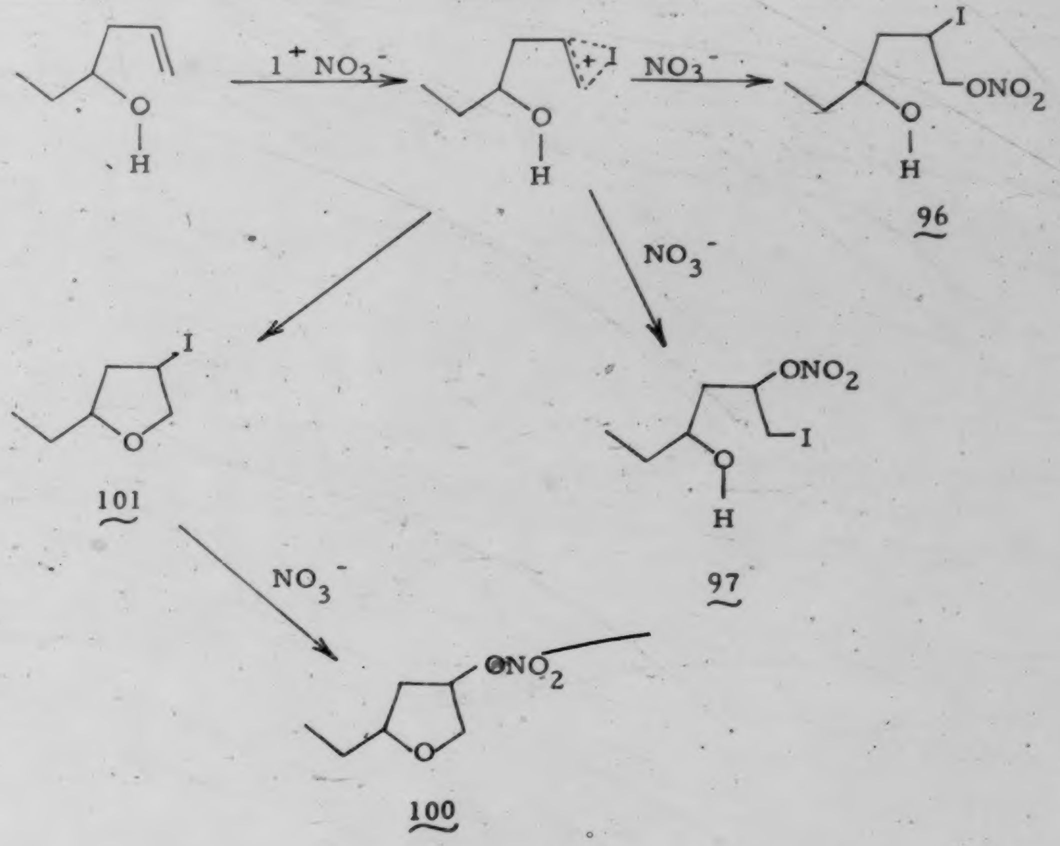


100

isolated in 30% yield together with the isomeric iodonitrates 96 and 97.

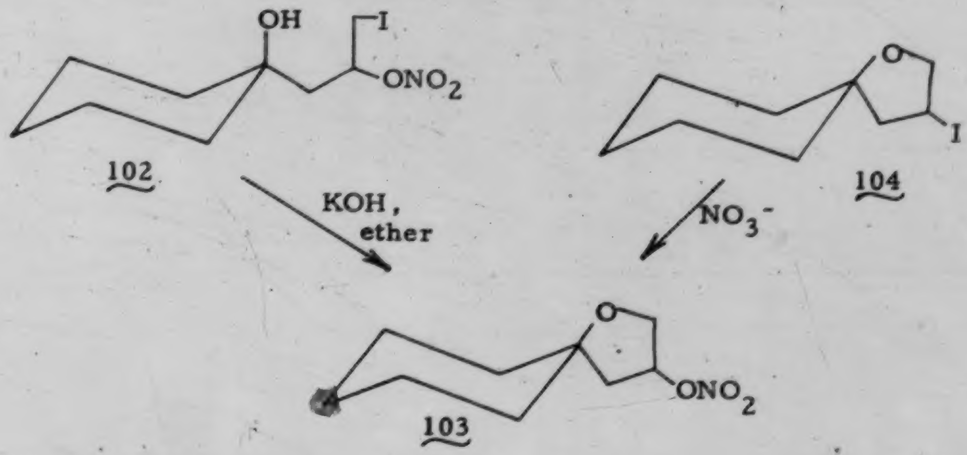
Treatment of the mixture of 96 and 97 with *sym*-collidine under conditions comparable with the formation of 100 and for up to 72 h. produced no reaction, thus discounting their intermediacy in the formation of 100. This suggests that the latter is formed by hydroxy-group attack on the intermediate iodonium ion followed by displacement of iodide (Scheme 5). This reaction parallels the displacement of the secondary iodide in compound 101 by pyridine in the formation of compound 99. Despite the low nucleophilicity of the nitrate ion[158,159], the displacement of secondary iodide from compound 101 would be favored by the much greater leaving ability of iodide (300 times that of nitrate[160]), reflecting the low C-I bond dissociation energy[161], and by the fact

Scheme 5



that the concentration of nitrate ions during the formation of 100 will be far in excess of that in the formation of 101. In addition the known propensity of iodide ion towards charge-transfer complexation[162,163] with pyridinium salts may assist in its departure.

Reaction of 1-allylcyclohexanol, a system where disubstitution on the hydroxy-bearing carbon should facilitate cyclization, with iodonium nitrate in chloroform-pyridine gave a normal addition product 102 in 55% yield. The Markovnikov nature of the addition was evident from the n.m.r. spectrum which showed absorptions at $\delta_{TMS}(CDCl_3)$: 3.4 (d) and 5.23 (quintet), characteristic of $-CH_2I$ and $-CH-ONO_2$ respectively. In addition to the normal addition product a spiro-ether was isolated in 10% yield, which proved to be 103 and not the expected product 104. This was confirmed by base-catalyzed cyclization of



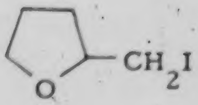
compound 102 to the spiro-ether 103, which was characterized by its n.m.r. and i.r. spectra and elemental analysis. A small amount of pyridinium salt was also isolated from the above addition reaction. It was difficult to make any conclusion as to the structure of the compound(s).

The formation of spiro-ether 103 in the addition of iodonium nitrate to 1-allylcyclohexanol is explicable on the basis of Scheme 5 outlined for the reaction of iodonium nitrate with hex-5-en-3-ol.

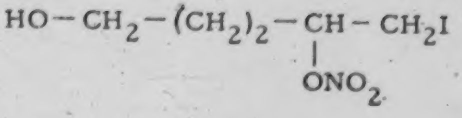
In contrast to the behaviour of 1-allylcyclohexanol towards iodonium nitrate in chloroform-pyridine, its reaction in chloroform-sym-collidine was rather surprising in that only the normal addition product 102 was formed and no cyclic ether could be detected. Also, the reaction was considerably slower and was incomplete even after 24 h. whereas reaction in chloroform-pyridine was complete in less than 3 h. The reason for this exceptional behaviour is not clear.

Reactions with 2-Allylphenols, Bis-Homoallylic Alcohols and Higher Olefinic Alcohols.

Olefinic compounds which can give rise to five- or six-membered cyclic structures by neighboring group participation in the addition of electrophilic reagents are generally expected to follow this path in preference to other reaction pathways as exemplified by the formation of five-membered cyclic ethers[137] and lactone[164] in the electrophilic addition of iodine to pent-4-en-1-ol and 4-pentenoic acid respectively. Addition of iodonium nitrate in chloroform-pyridine to pent-4-en-1-ol gave as the major product 2-iodomethyltetrahydrofuran 105 in 60% yield. In addition a small amount (6%) of isomeric hydroxy-iodoalkyl nitrates 106 and 107 was produced in a ratio of approximately 9:1, as determined by comparing the intensities of $-CH-ONO_2$ and $-CH_2-ONO_2$ absorptions in the n.m.r. spectrum. The i.r. spectrum showed intense hydroxy and nitrate absorptions. No isolable yield of iodopyridinium nitrate was formed in this reaction.

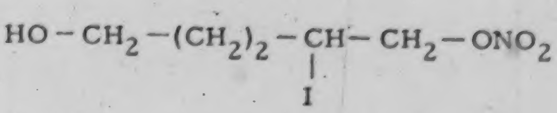


105



$$HO-CH_2-(CH_2)_2-\underset{ONO_2}{\underset{|}{CH}}-CH_2I$$

106

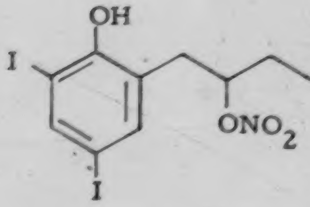


$$HO-CH_2-(CH_2)_2-\underset{I}{\underset{|}{CH}}-CH_2-ONO_2$$

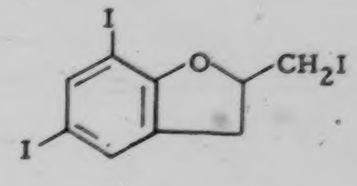
107

The structure of 105 was evident from the n.m.r. and i.r. spectra. The i.r. spectrum showed no hydroxyl absorption. The cyclic ether and the iodonitrate esters fraction were readily separable by chromatography on florisil.

As indicated in Chapter II, in the reaction between allylphenols and iodonium nitrate, no addition to the double bond takes place until all the available positions, *ortho* and *para* to the hydroxy group, are substituted with iodine; subsequently addition occurs readily. Thus 2-allylphenol on reaction with three molar equivalents of iodonium nitrate in chloroform-pyridine gave a normal addition product 108 in 13% yield and a cyclized product (33.5%) to which structure 109 is assigned. The two compounds were readily separable by chromatography on florisil. The regiochemistry of 108 was evident from the n.m.r. spectrum which showed characteristic absorptions for the

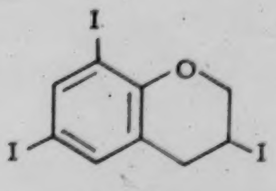


108



109

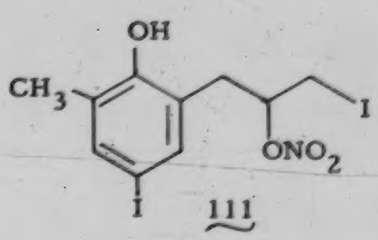
-CH$_2$I and -CH-ONO$_2$ groups at δ_{TMS}(CDCl$_3$): 3.33 and 5 to 5.5 respectively. For the cyclic product, although the alternative structure 110 is a distinct possibility, structure 109 is preferred mechanistically.



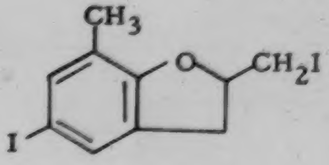
110

Attempted hydrogenolysis of the -CH$_2$I group with lithium aluminum hydride in ether at room temperature results in removal of iodine on the aromatic ring and cleavage of the five-membered ring together with the expected hydrogenolysis.

The possibility that 109 might arise from 108 by displacement of nitrate by the phenolic hydroxy group after the initial addition, was discounted by performing an addition to 2-allyl-6-methylphenol. Even after 24 h the same type of products, 111 and 112, were isolated in almost the same ratio (15% and 33.5% respectively).

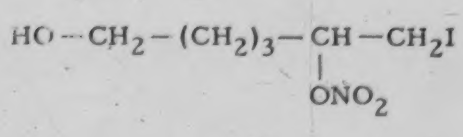


111



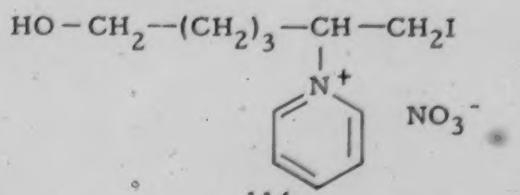
112

As the distance between the olefinic centre and the neighboring hydroxy group increases the propensity for participation decreases, as evidenced by the addition of iodonium nitrate to hex-5-en-1-ol. In chloroform-pyridine the major products isolated were the hydroxy-iodoalkyl nitrate 113 and the pyridinium salt 114 formed in 21% and 39% yields respectively. In both cases the regioisomers of



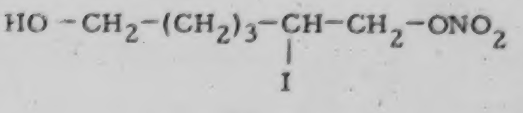
$HO-CH_2-(CH_2)_3-\underset{ONO_2}{\underset{|}{CH}}-CH_2I$

113



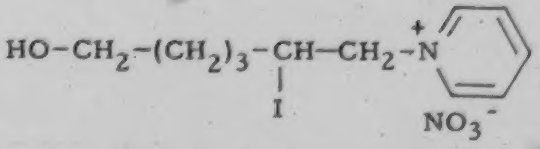
114

113 and 114 namely 115 and 116 could not be dectected in the n.m.r.



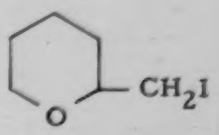
$HO-CH_2-(CH_2)_3-\underset{I}{\underset{|}{CH}}-CH_2-ONO_2$

115



116

spectra of the products. In this respect this addition resembles the addition of iodonium nitrate to 1-hexene where the Markovnikov addition products were formed exclusively. In addition to 113 and 114 a cyclic ether, 2-iodomethyl tetrahydropyran 117 was formed in 17% yield.



117

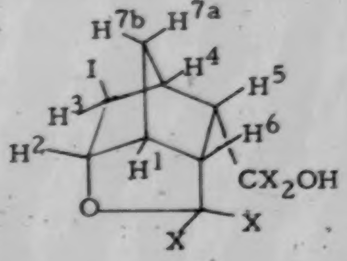
The behaviour of pent-4-en-1-ol and hex-5-en-1-ol towards iodonium nitrate is consistent with their behaviour towards bromine and iodine in that the propensity for participation by a neighboring hydroxyl group decreases if the resulting cyclic structure is six-membered rather than five-membered[137b].

Reactions with Bicyclic Olefinic Alcohols.

The behaviour of bicyclic olefinic alcohols towards iodonium nitrate was examined. It was expected that in such rigid ring systems participation by the neighboring hydroxy group will be preferred to other modes of reaction namely addition and/or rearrangement provided the participating group has the correct stereochemistry and the resulting ring system is stable.

The three isomeric 5-norbornene-2,3-dimethanols namely, endo-cis-5-norbornene-2,3-dimethanol, exo-cis-5-norbornene-2,3-dimethanol and trans-5-norbornene-2,3-dimethanol were synthesized accoridng to Schemes 6 and 7[165].

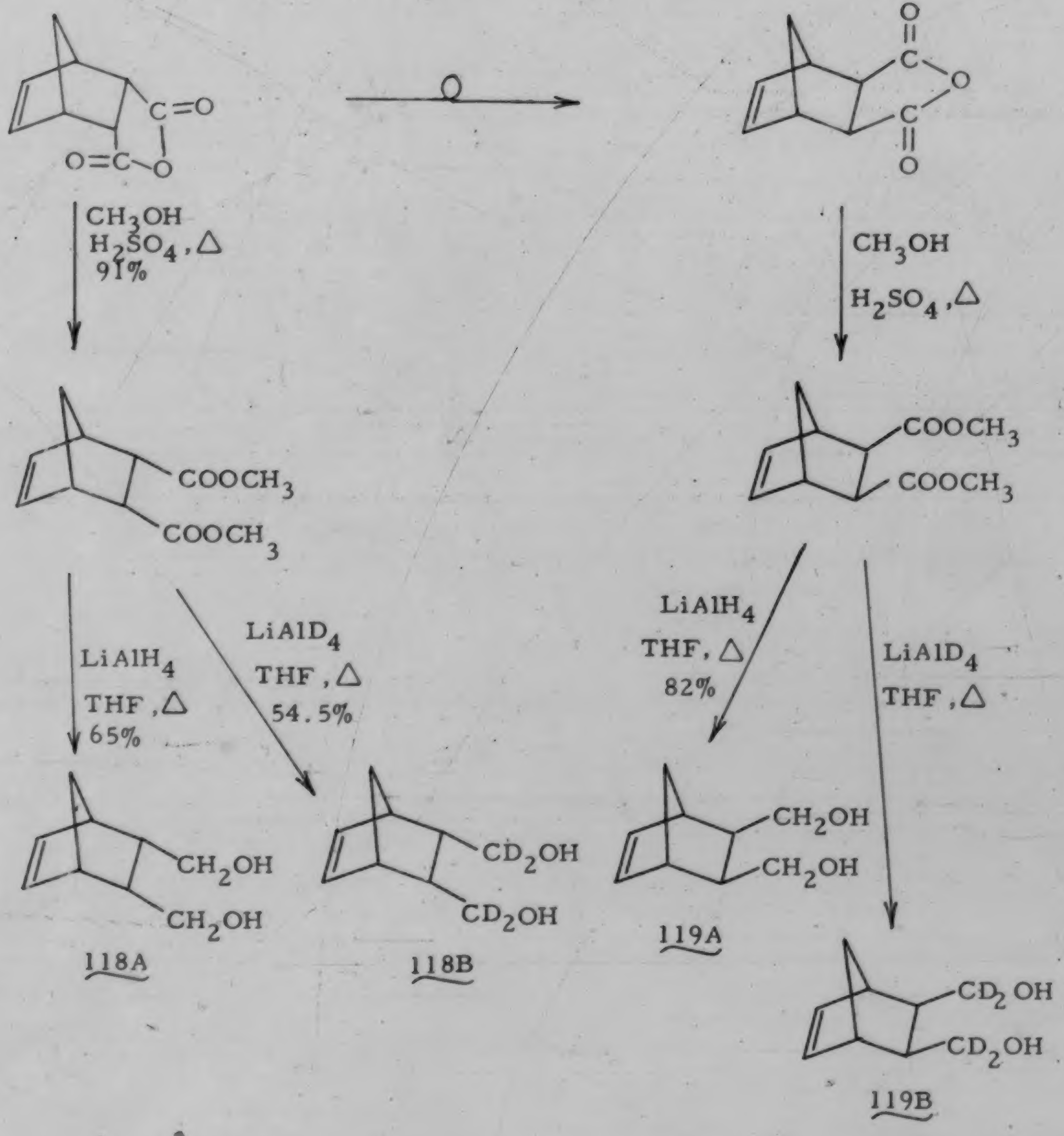
Reaction of endo-cis-5-norbornene-2,3-dimethanol 118A with iodonium nitrate in chloroform-pyridine produced a cyclized product 121A in 74% yield and a stoichiometric amount of pyridinium nitrate. Similarly addition of iodonium nitrate to the deuterated analog 118B (>95% deuterium) gave the corresponding cyclic ether 121B. Structural assignments for 121A and 121B are based on n.m.r. and i.r. spectra and elemental analysis. The n.m.r. spectrum showed only one exchangeable hydrogen. Assignments of the various absorptions in the n.m.r. spectra were made by comparison with other models and extensive decoupling. The n.m.r. spectrum of 121A



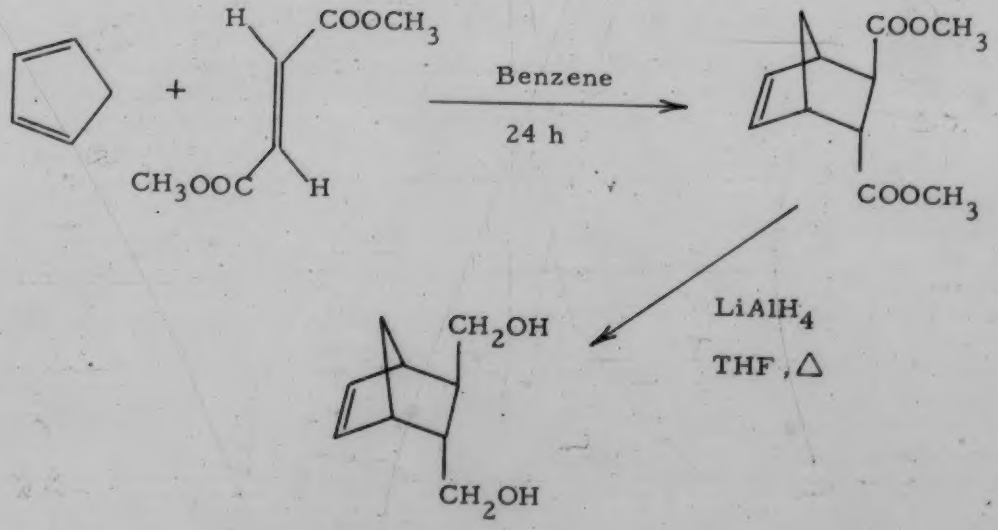
121A X=H

121B X=D

Scheme 6


C=O
O=C
O
Q
CH$_3$OH
H$_2$SO$_4$, Δ
91%
COOCH$_3$
COOCH$_3$
LiAlH$_4$
THF, Δ
65%
LiAlD$_4$
THF, Δ
54.5%
CH$_2$OH
CH$_2$OH
118A
CD$_2$OH
CD$_2$OH
118B
LiAlH$_4$
THF, Δ
82%
LiAlD$_4$
THF, Δ
CH$_2$OH
CH$_2$OH
119A
CD$_2$OH
CD$_2$OH
119B

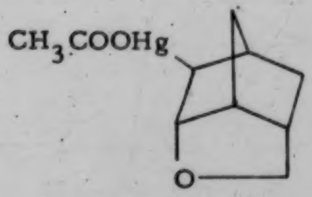
Scheme 7


H
COOCH$_3$
CH$_3$OOC
H
Benzene
24 h
COOCH$_3$
COOCH$_3$
LiAlH$_4$
THF, Δ
CH$_2$OH
CH$_2$OH

120

showed δ_{TMS} (CDCl$_3$): 4.82 (d, 1H, H^2, $J_{1,2}$=5.5 Hz, $J_{2,3}$=0 Hz); 3.8 (d, 1H, H^3, $J_{3,7a}$=2.5 Hz); 3.4-3.8 (m, 4H, 2 -CH_2-O); 2.68 (m, 1H, H^1); 2.1-2.5 (m, 4H, H^4, H^5, H^6, H^{7b}); 1.76 (m, 1H, H^{7a}); 2.5 (s, 1H, -OH). The n.m.r. spectrum of 121B differed from that of 121A in that the multiplet at δ 3.4-3.8 disappeared and some splitting disappeared in the region δ 2.1-2.35 corresponding to H^5 and H^6.

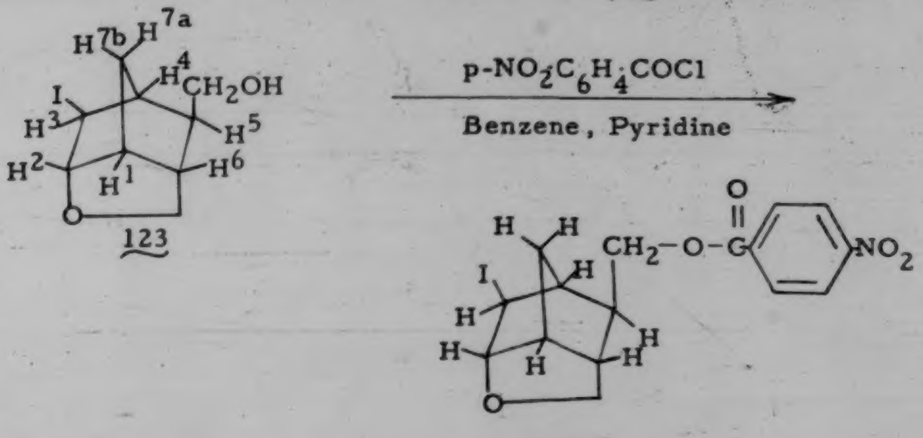
One interesting feature of the n.m.r. spectrum of 121A and 121B is the absence of spin-spin coupling between H^2 and H^3. Similar protons in other comparable systems[166-169], for example 122, show a coupling constant of approximately 2.2 to 2.3 Hz. H^2 is coupled to H^1 (J=5.5 Hz) in the case of 121.



122

The multiplet at δ 1.76 is assigned to H^{7a} because it is coupled to H^3 (J=2.5 Hz) via W-coupling. In other systems such protons show a coupling constant of approximately 3-4 Hz[48c].

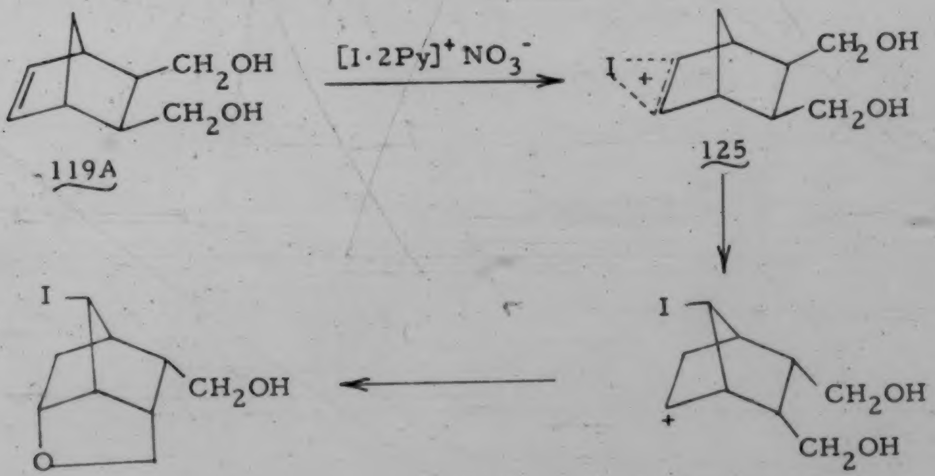
Reaction of iodonium nitrate with trans-5-norbornene-2,3-dimethanol 120 in chloroform-pyridine gave the cyclized product 123 in 86% yield together with a corresponding amount of pyridinium nitrate. Compound 123 contained only one hydroxyl group as shown by the formation of a mono-para-nitrobenzoyl derivative 124 in 70% yield, which was characterized by its n.m.r. and i.r. spectra and elemental analysis. The n.m.r. spectrum of 123 showed H^2 at $\delta_{TMS}(CDCl_3)$: 4.73 (d, 1H, $J_{1,2}$=5 Hz) and H^3 at δ 3.65 (d, 1H, $J_{3,7a}$=2.3 Hz). Again no coupling was observed between H^2 and H^3.


H7b
H7a
H4
CH2OH
I
H3
H5
H2
H1
H6
O
p-NO2C6H4COCl
Benzene, Pyridine
O
H
H
CH2–O–C
NO2
I
H
H
H
H
H
H
O

123

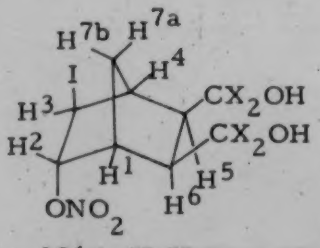
124

The behaviour of *exo*-*cis*-5-norbornen-2,3-dimethanol 119 towards iodonium nitrate was examined. In this compound, since the two hydroxymethyl groups are in an *exo*-*cis*-configuration, no participation could be expected unless the initially formed iodonium ion intermediate 125 undergoes skeletal rearrangement followed by subsequent cyclization.



In the event reaction of iodonium nitrate with 119A gave a mixture of products from which the major product 126A was isolated in 40% yield by chromatography of the crude reaction product on florisil. The formation of a number of products indicates skeletal rearrangement or hydride transfer reaction as observed for the addition of iodonium nitrate to norbornene. The minor products could not be identified. The structure of 126A was determined from a comparison of its n.m.r. spectrum with that of 29, obtained from the reaction of iodonium nitrate with norbornene. The i.r. spectrum showed intense absorption at 1630 cm^{-1} indicating the presence of a ONO$_2$ group.

The assignments of the various absorptions in the n.m.r. spectrum were made by extensive decoupling and by comparison of the spectrum with that of 126B prepared from the deuterium analog of 119A, namely 119B (>95% D). Thus the n.m.r. spectrum of 126B


H7b
H7a
I
H4
H3
CX2OH
H2
CX2OH
H1
H5
ONO2
H6

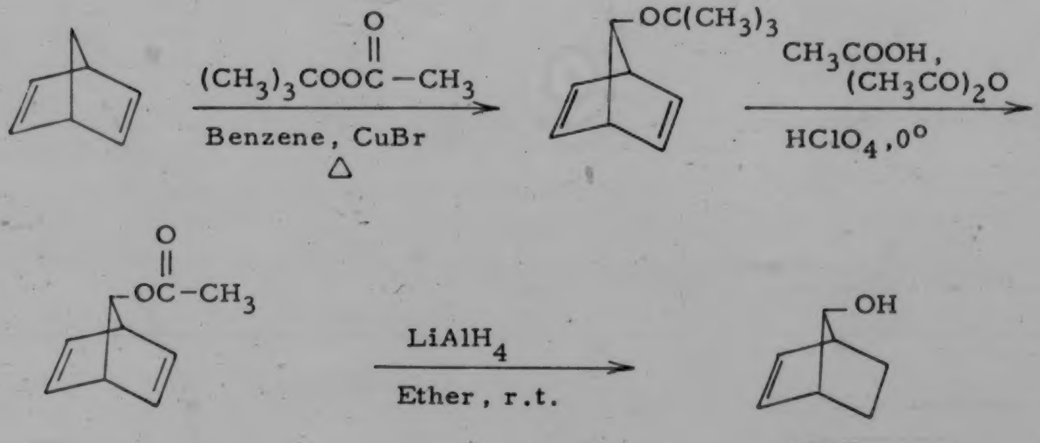
126A X=H

126B X=D

showed $\delta_{TMS\ (CDCl_3)}$: 5.5 (q, 1H, H^2, $J_{2,3}$=2.8 Hz, $J_{1,2}$=2 Hz); 3.82 (t, 1H, H^3, $J_{2,3}=J_{3,7a}$=2.8 Hz). The methylene signal of the hydroxymethyl groups in 126A appeared as a multiplet at δ 3.3 to 4.

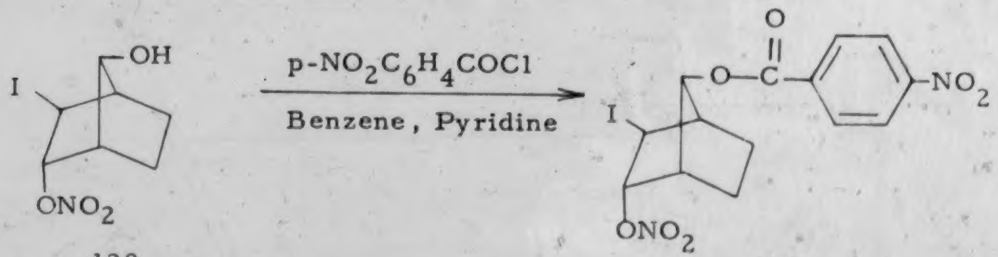
Anti-7-Norbornenol 127, prepared according to Scheme 8[170], on reaction with iodonium nitrate in chloroform-pyridine gave 128 as the sole product indicating a preference for addition. Compound 128

Scheme 8


(CH3)3COOC(=O)−CH3
Benzene, CuBr
Δ
OC(CH3)3
CH3COOH,
(CH3CO)2O
HClO4, 0°
OC(=O)−CH3
LiAlH4
Ether, r.t.
OH

127

was characterized as its *para*-nitrobenzoyl derivative 129.

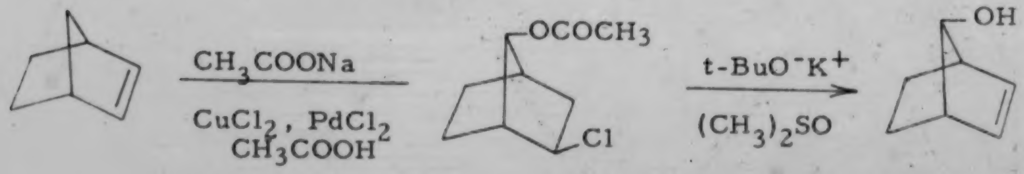

OH
I
ONO$_2$
p-NO$_2$C$_6$H$_4$COCl
Benzene, Pyridine
O
O—C
NO$_2$
I
ONO$_2$

128

129

In contrast to the behaviour of anti-7-norbornenol, *syn*-7-norbornenol 130, prepared according to Scheme 9[171], on reaction with iodonium nitrate gave a mixture of several products as shown by the n.m.r. spectrum of the crude reaction products. None of the products could be characterized. The above result is consistent with rearrangements in such systems. Here the reaction was comparatively slower indicating the steric hindrance by the hydroxyl group.

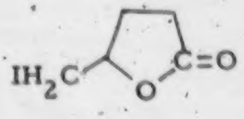
Scheme 9


CH$_3$COONa
CuCl$_2$, PdCl$_2$
CH$_3$COOH
OCOCH$_3$
Cl
t-BuO$^-$K$^+$
(CH$_3$)$_2$SO
OH

130

Miscellaneous Reactions.

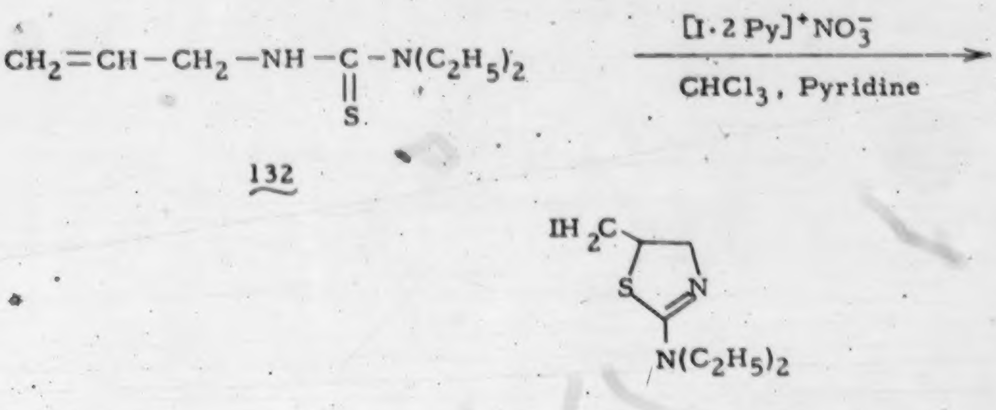
Like hydroxy groups, the carboxyl group can also participate in iodonium nitrate additions if such participation can lead to five- or six-membered ring structures. An example is provided by the addition of iodonium nitrate to 4-pentenoic acid which gave the iodolactone 131 along with the stoichiometric amount of pyridinium nitrate. No other product could be isolated in this reaction. Compound 131 has also been



131

obtained in the addition of iodine[164] and iodine cyanide[35] to 4-pentenoic acid.

An example of participation by a neighboring sulfur is provided in the addition of iodonium nitrate to the allylthiourea **132**, which gave a cyclized product tentatively assigned as the thiazoline **133**.



$CH_2{=}CH{-}CH_2{-}NH{-}\underset{\underset{S}{\|}}{C}{-}N(C_2H_5)_2 \xrightarrow[CHCl_3,\ Pyridine]{[I\cdot 2\,Py]^+NO_3^-}$

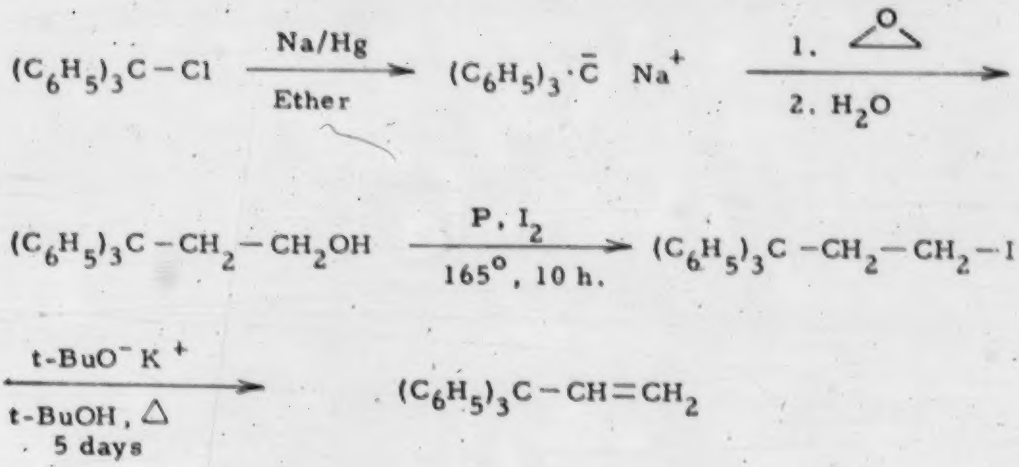
132

133

As indicated in Chapter II, for the addition of iodonium nitrate to norbornene and norbornadiene, rearrangements as a result of σ- and π-bond participation are possible in suitable substrate olefins. Hassner and Teeter reported phenyl participation and subsequent migration during the addition of iodine azide and iodine isocyanate to 3,3,3-triphenylpropene. A comparable experiment with iodonium nitrate both in chloroform-pyridine and chloroform-*sym*-collidine produced no reaction in contrast to the ready addition to *tert*.-butylethylene and (*Z*) and (*E*)-4,4-dimethylpent-2-enes (see Chapter IV).

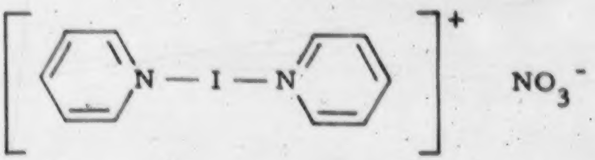
[3,3,3-Triphenylpropene was synthesized according to Scheme 10[172, 106]]. This unexpected result may indicate steric hindrance for the

Scheme 10


$(C_6H_5)_3C-Cl$
Na/Hg
Ether
$(C_6H_5)_3\cdot\bar{C}\ Na^+$
1.
2. H_2O
$(C_6H_5)_3C-CH_2-CH_2OH$
P, I_2
165°, 10 h.
$(C_6H_5)_3C-CH_2-CH_2-I$
t-BuO⁻ K⁺
t-BuOH, △
5 days
$(C_6H_5)_3C-CH=CH_2$

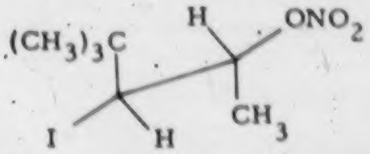
approach of the bulky complex 134 to the 3,3,3-triphenylpropene.

Although the reactive species in iodonium nitrate additions can be represented as INO_3, the iodine is complexed to two pyridine molecules in this solvent. The complex 134 may be isolated as a crystalline solid which is soluble in polar solvents and stable in the absence of moisture and light.

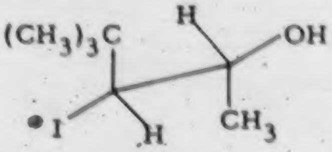


134

(E)-4,4-Dimethylpent-2-ene with an equivalent of the complex 134 in dimethylsulfoxide, which was not dried gave the iodonitrate 135 and the iodohydrin 136 stereospecifically (see Chapter IV). But in

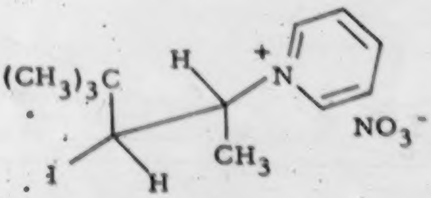


135



136

rigorously dried dimethylsulfoxide only compound 135 was formed indicating that the iodohydrin 136 results from nucleophilic attack of water on the intermediate iodonium ion. The addition with the complex can also be performed in anhydrous acetonitrile. Thus (*E*)-4,4-dimethylpent-2-ene gave compound 135 and a trace of the corresponding iodopyridinium nitrate 137.



137

Our attempts to determine the structure of the complex 134 by X-ray crystallography were not successful due to its instability. However, the structure of iodine perchlorate as its di-*sym*-collidine complex has been determined[173]. Figure 1 shows the structure of one form of the complex. The studies show the presence of distinct covalent bond between nitrogen and iodine with the N-I-N bond angle of 177 ± 1° for one form and 180° for the other. Accordingly the pyridine complex of iodonium nitrate may also be expected to have a similar structure as in 134.

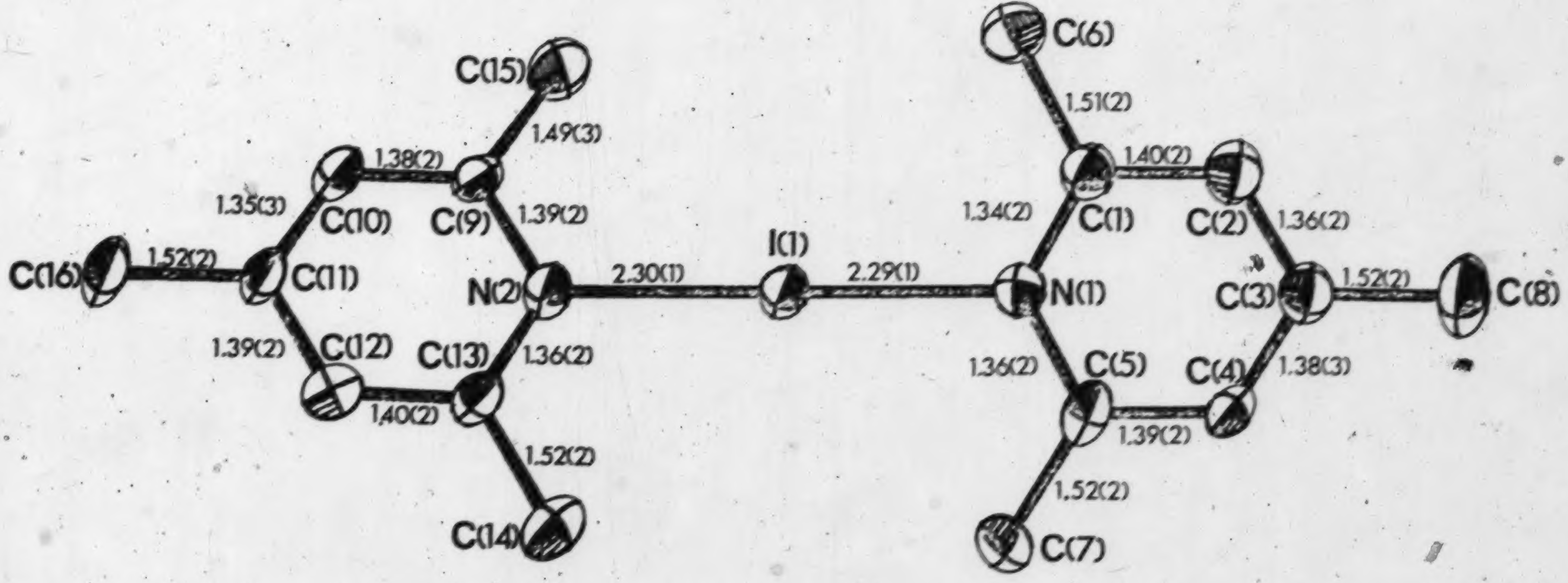
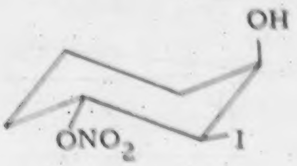

C(15)
1.49(3)
1.38(2)
1.35(3)
C(10)
C(9)
1.39(2)
C(16)
1.52(2)
C(11)
N(2)
2.30(1)
I(1)
2.29(1)
1.39(2)
C(12)
C(13)
1.36(2)
1.40(2)
1.52(2)
C(14)
C(6)
1.51(2)
1.40(2)
1.34(2)
C(1)
C(2)
1.36(2)
N(1)
C(3)
1.52(2)
C(8)
1.36(2)
C(5)
C(4)
1.38(3)
1.39(2)
1.52(2)
C(7)

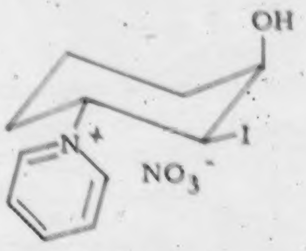
Figure 1. X-ray Crystallographic Structure of Iodonium Perchlorate-sym-Collidine Complex.

Stereochemical Directing Influence of Neighboring Hydroxyl Groups in the Addition of Pseudohalogens to Cycloalk-2-en-1-ols.

Addition of iodonium nitrate to cyclohex-2-en-1-ol in chloroform-pyridine gave an iodonitrate ester 138 in 36% yield and an iodopyridinium nitrate 139 in 29% yield. Examination of the appropriate coupling constants in the n.m.r. spectrum of 138 showed it to be 3-hydroxy-2-iodocyclohexyl nitrate with the stereochemistry shown in which the hydroxy group is axial. N.m.r. analysis of the iodopyridinium nitrate 139 does not provide enough information to decide if there are one or two isomers or to determine the stereochemistry. Assuming both the iodonitrate ester and the iodopyridinium salt are formed from the same intermediate iodonium ion, structure 139 is proposed for the salt. Parallel reaction of iodonium nitrate in chloroform-*sym*-collidine with cyclohex-2-en-1-ol gave 138 in 55% yield.

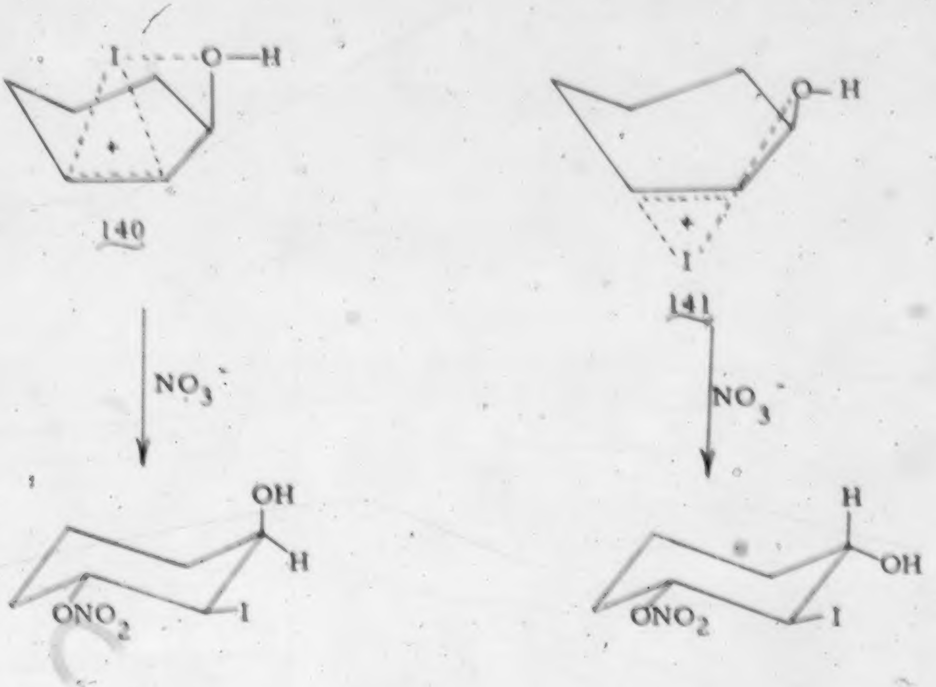


138



139

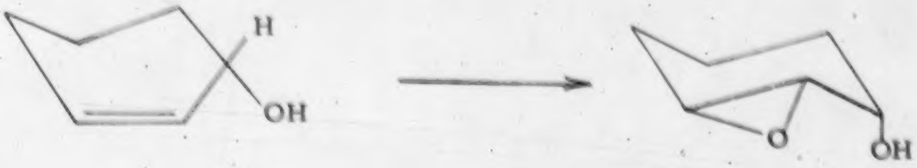
Consideration of the stereochemistry of the two possible intermediates 140 and 141 favors an intermediate of the type 140 and proves that the iodonium ion is formed *cis* to the hydroxyl group. This is in agreement with the observed stereochemistry of epoxidation of cyclohex-2-en-1-ols in which the oxirane ring is formed *cis* to the hydroxy group[174,175]. Apparently the epoxidation reagent becomes



140

141

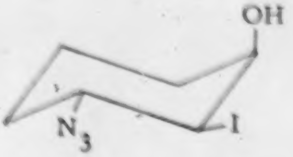
associated in some way with the hydroxy group in the molecule prior to attacking the double bond and is therefore constrained to approach



the latter from that side of the ring which bears the hydroxy group.

The above result prompted us to investigate the stereochemical directing influence of hydroxy groups in the addition of other pseudohalogens to cyclohex-2-en-1-ol and also in the addition of iodonium nitrate to cycloalk-2-en-1-ols of various ring sizes.

Reaction of iodine azide with cyclohex-2-en-1-ol produced an unstable adduct in 86% yield. The i.r. spectrum of the adduct showed strong absorption at 2100 cm^{-1} indicating the presence of azide group in the molecule. The n.m.r. spectrum showed the following significant absorptions $\delta_{TMS\ (CDCl_3)}$: 4.3 (q, 1H, -CH-I, J= 8.5 Hz and 2.5 Hz); 3.7-4.15 (m, 2H, -CH-OH and -CH-N_3). On the basis of the n.m.r. spectrum structure 142 is assigned to the adduct, which



142

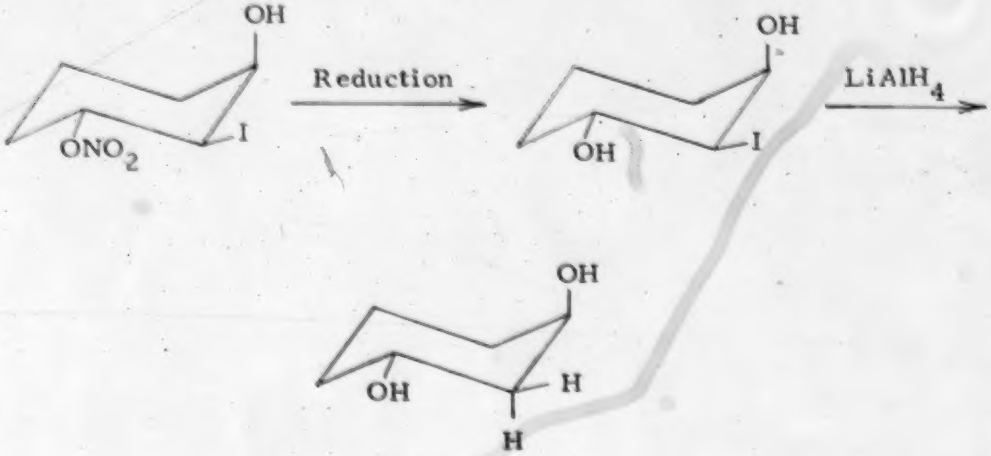
is derived from an intermediate iodonium ion formed cis to the hydroxy group.

Addition of iodine monochloride to cyclohex-2-en-1-ol gave a product in about 90% yield, but no stereochemical information could be gathered from the n.m.r. spectrum. Addition of iodine isocyanate produced only tarry material and no identifiable product was isolated.

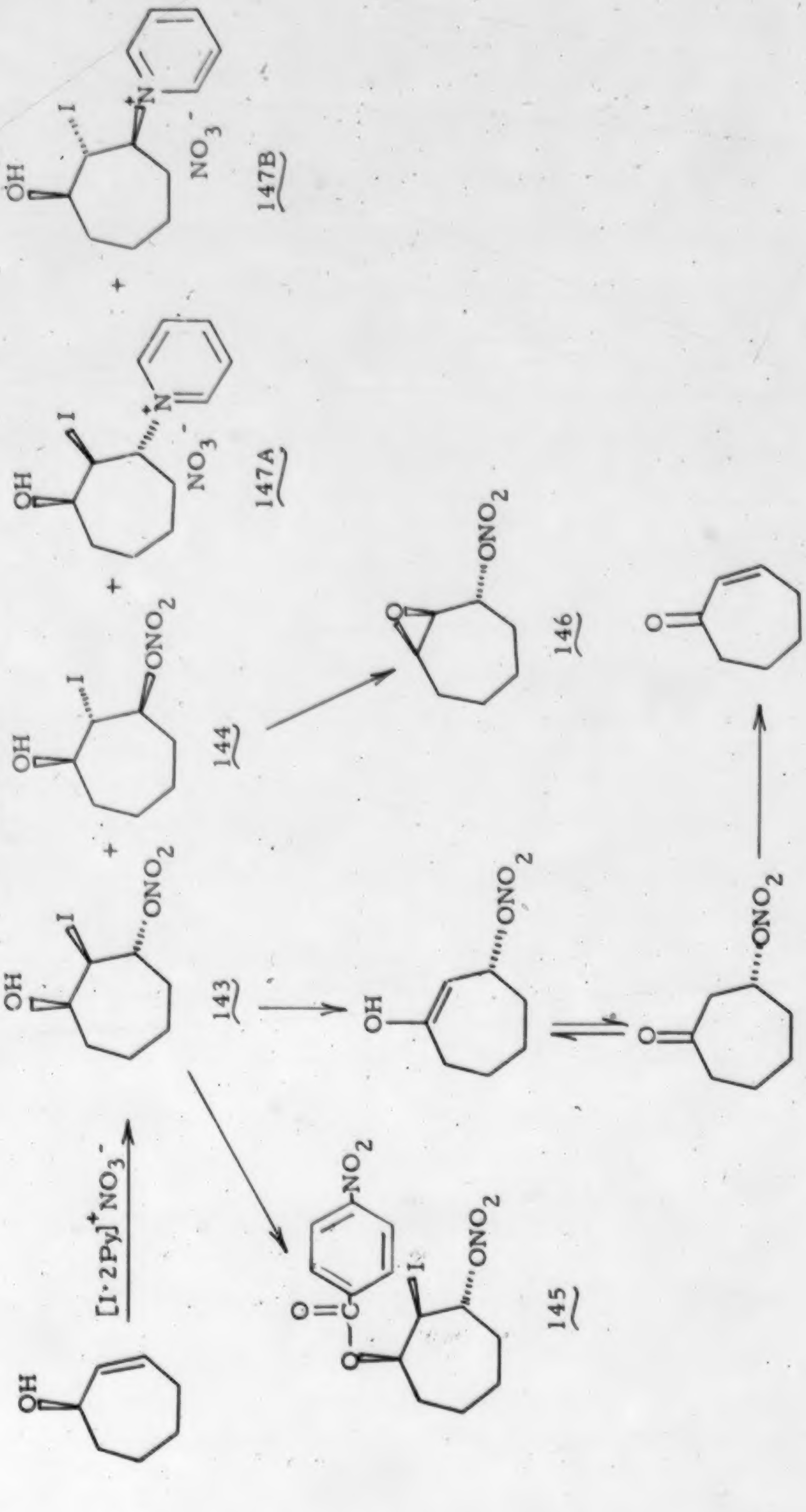
Cyclohept-2-en-1-ol with iodinium nitrate produced four products. The two iodonitrate esters were formed in a combined yield of 59% and in a ratio of approximately 80:20 (obtained by comparing the n.m.r. intensity of -CH-I of the major product with the total intensity of -CH-ONO_2 at $\delta_{TMS(CDCl_3)}$: 5.2-5.6). The major product is assigned structure 143 in which the iodine is cis to the hydroxyl group, and the minor product as 144. The major product had the -CH-I absorption in the n.m.r. spectrum at $\delta_{TMS\ (CDCl_3)}$: 4.57 (q), with coupling constants of 2.25 Hz and 6.75 Hz. The n.m.r. spectrum of the cycloheptene-iodonium nitrate adduct showed absorptions at $\delta_{TMS\ (CDCl_3)}$: 4.33 (sextet, 1H, -CH-I, $J_{a,a}$=7 Hz, $J_{a,e}$=5 Hz), 5.36 (sextet, 1H, -CH-ONO_2, $J_{a,a}$=7 Hz, $J_{a,e}$=3.5 Hz). This indicates that in 143 the hydroxy group is pseudo-axial and iodine and nitrate groups equatorial. Esterification of the hydroxyl group with *para*-nitrobenzoyl chloride in the presence of pyridine allowed separation of the major product as a crystalline derivative 145 which had in the n.m.r. spectrum absorptions at $\delta_{\text{TMS (CDCl}_3)}$: 4.77 (q, 1H, CH-I, J=2.5 Hz and 6.5 Hz); 4.96 (m, 1H, -CH-O-); 5.5 (m, 1H, -CH-ONO_2). Treatment of the mixture of iodonitrate esters with potassium hydroxide in ether produced cycloheptenone as the major product by elimination of both hydrogen iodide and nitric acid from 143 and another compound which is assigned the epoxy-nitrate structure 146 derived from 144 by base catalyzed cyclization. The transformations are illustrated in Scheme 11.

The iodopyridinium nitrate salts were formed in 27% and 8% yields respectively. They were easily separated by fractional crystallization from ethanol. An unequivocal assignment of their structures can not be made at this point.

Our attempts to establish the structures of iodonitrate esters 143 and 144 and similar compounds by chemical transformation as shown below to known compounds were unsuccessful. Thus



Scheme 11

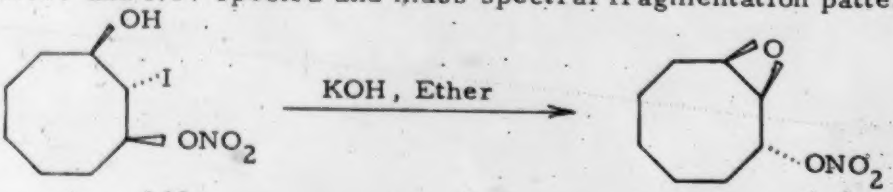

OH
$[I \cdot 2Py]^+NO_3^-$
OH
I
ONO_2
143
+
OH
I
ONO_2
144
+
OH
I
N^+
NO_3^-
147A
+
OH
I
N^+
NO_3^-
147B
O
ONO_2
146
OH
ONO_2
O
ONO_2
O
O
O=C
I
NO_2
ONO_2
145

attempted conversion of the nitrate group in **138** to the alcohol function by catalytic reduction over palladium-carbon in the presence of various organic tertiary bases gave cyclohexanol. Lithium aluminum hydride gave the same result. On the other hand hydrogenation in the presence of inorganic bases and zinc-copper couple hydrogenolysis in ethanol effected no change. Zinc-copper couple hydrogenolysis of the cyclooctenol-iodonium nitrate adduct (*vide infra*) in acetic acid resulted in the elimination of iodine and nitrate.

Reaction of iodonium nitrate with cyclooct-2-en-1-ol in chloroform-pyridine gave an iodonitrate ester in 60% yield. No iodopyridinium nitrate could be isolated in this case. The reaction was considerably slower and traces of cyclooctenol could be detected in the reaction mixture even after 24 h.

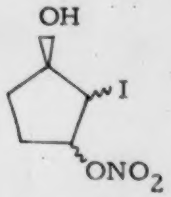
The assignment of structure **148** to the iodonitrate ester is based on a comparison of the coupling constants in the n.m.r. spectrum of **148** with those in the spectrum of the cyclooctene-iodonium nitrate adduct **37**. Thus the n.m.r. spectrum of **148** showed absorptions at δTMS ($CDCl_3$): 4.43 (t, 1H, -CHI, J=9 Hz); 5.3 (sextet, 1H, $-CH-ONO_2$, J=9 Hz and 4.5 Hz). The corresponding coupling constant $J_{CHI-CH-ONO_2}$ in the spectrum of **37** was 10 Hz. A coupling constant of 9 Hz indicates a *trans* configuration of iodine and hydroxyl groups.

Treatment of adduct **148** with potassium hydroxide in ether gave a cyclized product assigned as the epoxy-nitrate **149** on the basis of n.m.r. and i.r. spectra and mass spectral fragmentation pattern.

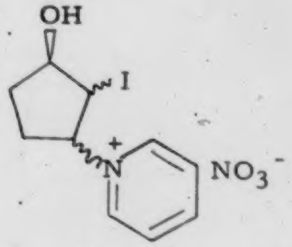


148 **149**

Cyclopent-2-en-1-ol with iodonium nitrate in chloroform-pyridine produced an iodonitrate ester 150 in 52% yield and the corresponding iodopyridinium nitrate 151 in 22% yield. No stereochemical information could be gathered from the n.m.r. spectra of the products and comparison with that of the cyclopentene-iodonium nitrate adducts. Treatment of the iodonitrate ester with base did not produce any cyclized product. This may indicate that the iodonium ion may be formed cis to the hydroxy group.



150



151

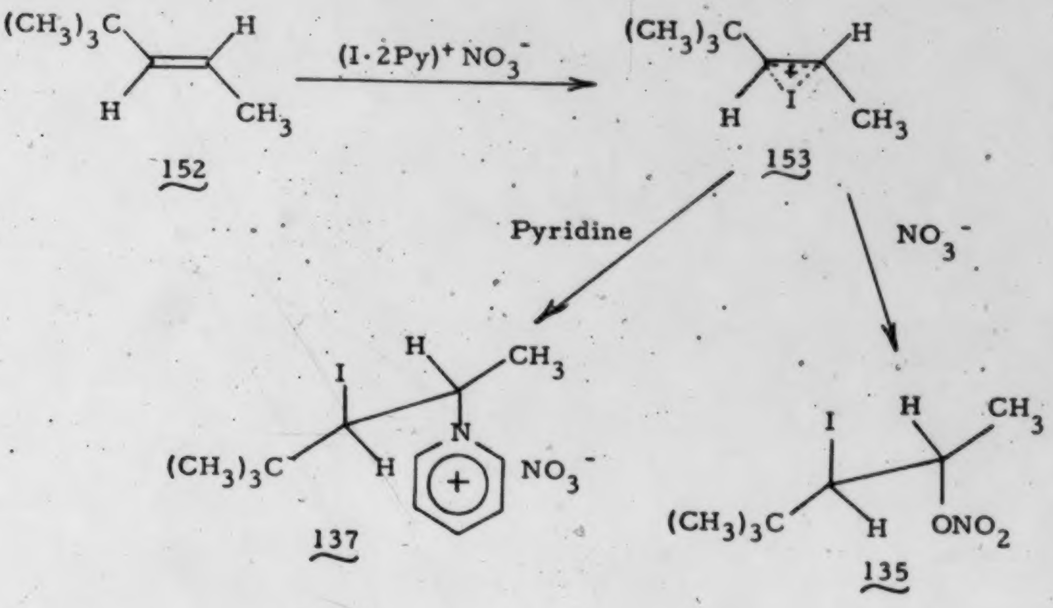
It is interesting to note the behaviour of these olefinic alcohols in electrophilic epoxidation reactions. Cyclohept-2-en-1-ol gave a mixture of cis and trans-3-hydroxycycloheptene oxides in a ratio of 2:1[176,177]. On the other hand cyclooct-2-en-1-ol gave the trans isomer stereospecifically[178]. No information is available on the stereochemistry of epoxidation of cyclopent-2-en-1-ol.

CHAPTER IV

Stereochemistry, Regiochemistry and Mechanism of the Addition of Iodonium Nitrate to Alkenes[179].

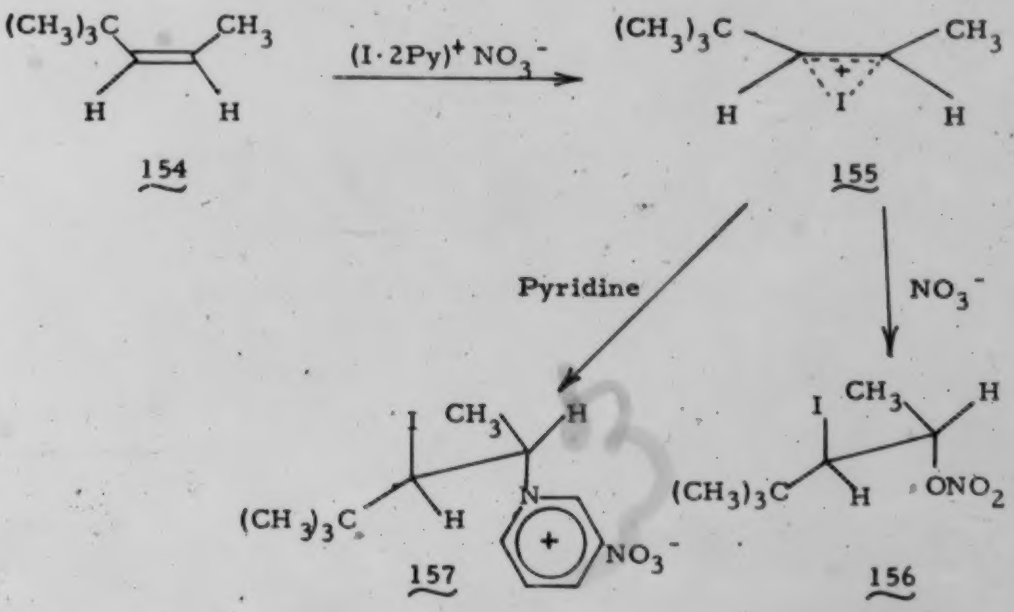
In Chapters II and III we have seen the reactions of iodonium nitrate with olefins of different structural types and also the effect of neighboring groups. It is evident that the scope of these reactions and the reactivity of iodonium nitrate are substantially different from those of other pseudohalogens. Hence it was necessary to examine the stereochemistry, regiochemistry and mechanism of iodonium nitrate additions in greater detail.

Pure (E)-4,4-dimethylpent-2-ene 152 was treated with an equivalent of iodonium nitrate in chloroform-pyridine affording a single stereoisomer of the iodonitrate ester 135 in a regiospecific (ONO_2-methyl) anti-Markovnikov addition in 76% yield together with the corresponding iodopyridinium nitrate 137 in 5% yield, which also subsequently proved to be stereospecific and regiospecific in its formation. The



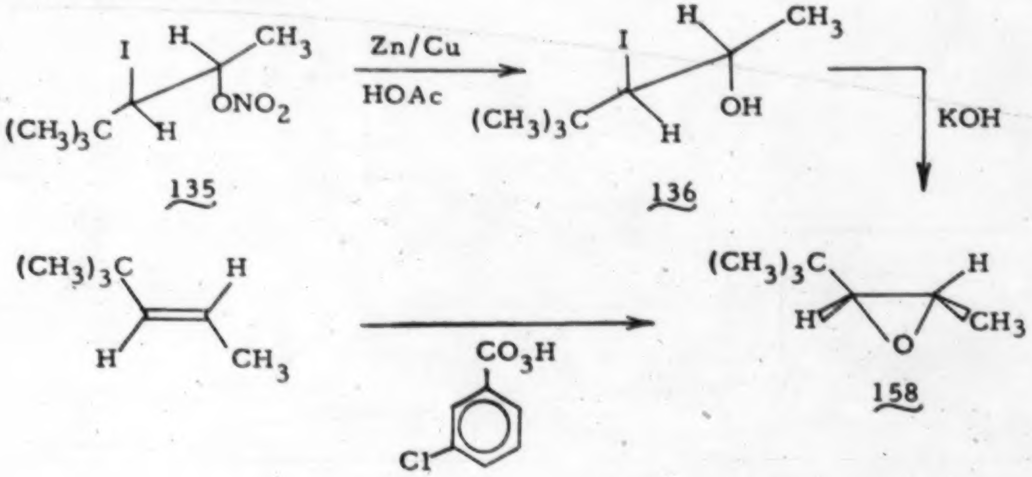
regiochemistry of the additions was assigned by reference to the n.m.r. spectra as described in Chapter II.

Similarly treatment of pure (Z)-4,4-dimethyl pent-2-ene 154 with iodonium nitrate afforded only one stereoisomerically pure iodonitrate ester 156 in 91.5% yield together with the iodopyridinium nitrate 157 in 5.5% yield. (No conformational preference is implied by the sawhorse projection formulas.)



The n.m.r. spectrum of 135 and 156 were quite distinct indicating stereospecific addition of iodonium nitrate to the above olefins. The methine hydrogens of 135 absorbed at $\delta_{\text{TMS (CDCl}_3\text{)}}$: 4.42 (d, 1H, J=2.75 Hz); and 4.8 (octet, 1H, J=6.2 Hz and 2.75 Hz), characteristic of -CH-I and -CH-ONO_2 methine hydrogens respectively while those for 156 absorbed at $\delta_{\text{TMS (CDCl}_3\text{)}}$: 3.99 (d, 1H, J=1.5 Hz), and 4.93 (octet, 1H, J=1.5 Hz and 6.15 Hz) respectively.

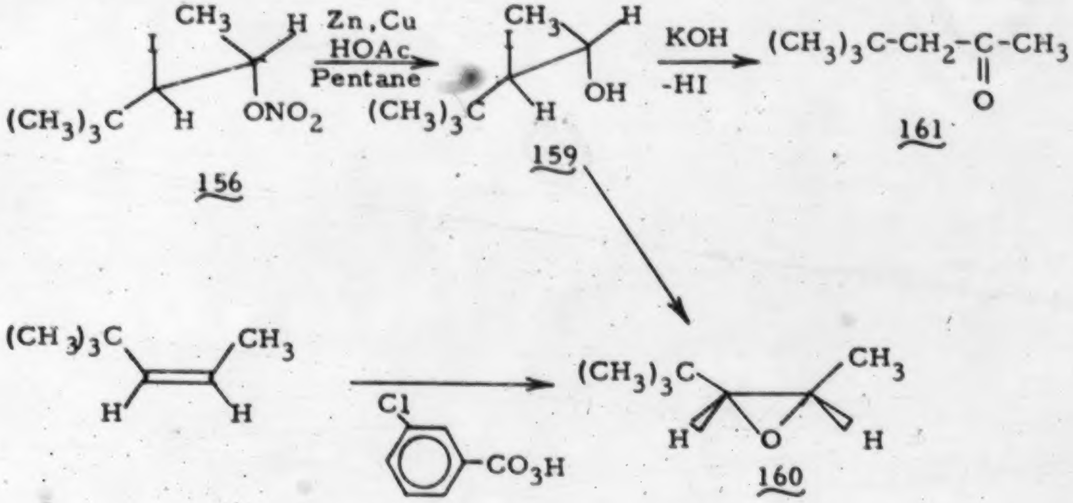
Zinc-copper couple reduction of iodonitrate ester 135 in acetic acid afforded the iodohydrin 136 in 29% yield. Treatment of iodohydrin 136 with powdered potassium hydroxide in anhydrous ether gave the (E)-epoxide 158 in 70% yield which was identical with the authentic (E)-epoxide prepared in 68% yield by the oxidation of pure (E)-4,4-dimethylpent-2-ene 152 with *meta*-chloroperbenzoic acid in methylene chloride.



Since electrophilic epoxidation of olefins by peracids is known to be *cis* stereospecific[180] and since zinc-copper couple hydrogenolysis of the nitrate grouping does not affect the configuration at the carbon atom, then this proves that 135 has the *erythro* configuration and thereby the addition of iodonium nitrate to (E)-olefin is stereospecifically *trans*.

Similar treatment of iodonitrate ester 156 with zinc-copper couple in acetic acid for preparation of the iodohydrin 159 was unsatisfactory since no appreciable amount of the desired compound was obtained. But it was found that dilution of the reaction mixture with an inert solvent such as pentane gave the iodohydrin 159 in 41% yield. Treatment of iodohydrin 159 with potassium hydroxide gave the (Z)-epoxide 160. In this case considerable base catalyzed elimination of the iodohydrin to give ketone, 4,4-dimethylpentan-2-one 161, accompanied ring closure to the epoxide 160. An authentic sample of (*Z*)-epoxide was synthesized by *meta*-chloroperbenzoic acid oxidation of (*Z*)-4,4-dimethylpent-2-ene in methylene chloride.

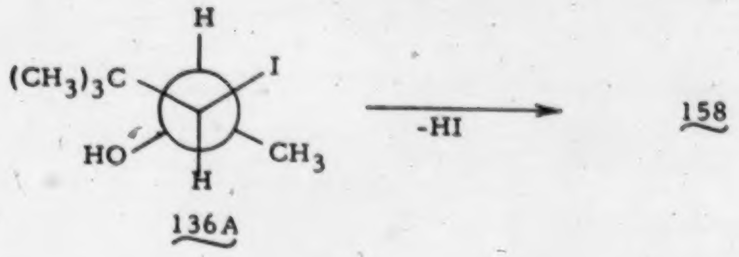
These observations conclusively prove that iodonitrate ester 156 has the *threo* configuration and therefore addition of iodonium

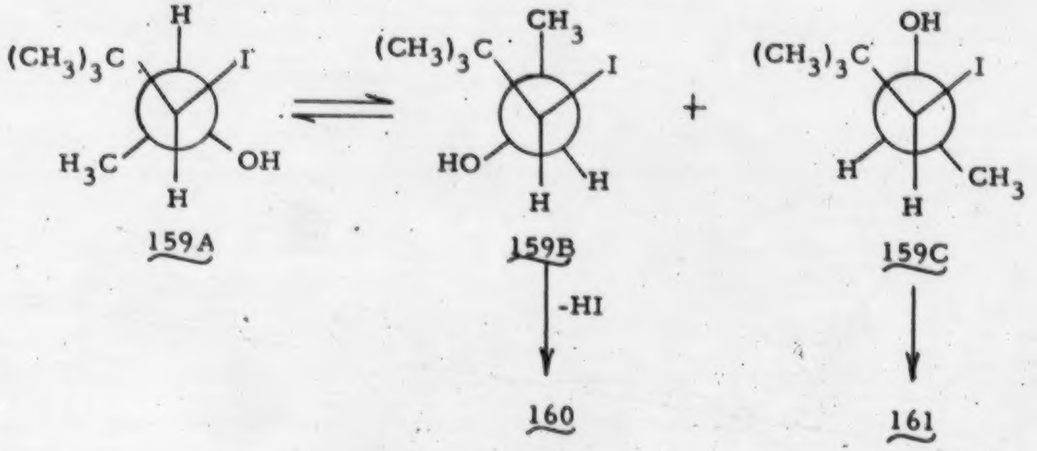


CH$_3$
H
I
(CH$_3$)$_3$C
H
ONO$_2$
156
Zn,Cu
HOAc
Pentane
CH$_3$
H
I
OH
(CH$_3$)$_3$C
H
159
KOH
-HI
(CH$_3$)$_3$C-CH$_2$-C-CH$_3$
O
161
(CH$_3$)$_3$C
CH$_3$
H
H
Cl
CO$_3$H
(CH$_3$)$_3$C
CH$_3$
H
O
H
160

nitrate to the (*Z*)-olefin is also stereospecifically *trans*.

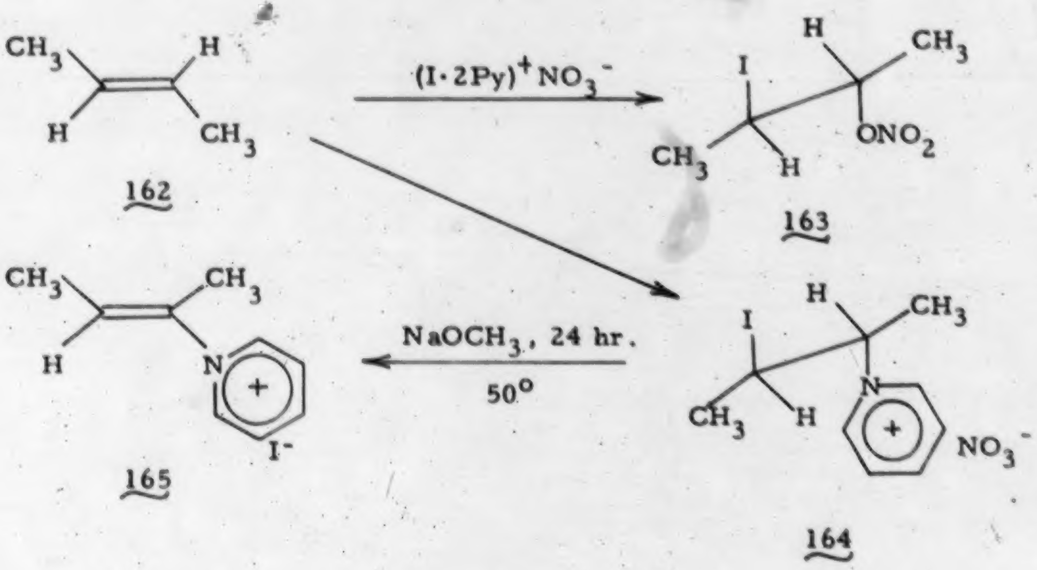
The relative ease of *trans* displacement of iodide from the *erythro*-iodohydrin 136 to form epoxide 158 compared with the slow formation of the (*Z*)-epoxide 160 from the *threo*-iodohydrin 159 indicates preferred conformations 136A for the former and 159A for the latter. Whereas no ketone is formed from 136A, 159A may rotate with equal facility to two conformers, 159B and 159C, comparable in energy giving rise to 160 and 161 in approximately equal proportion.

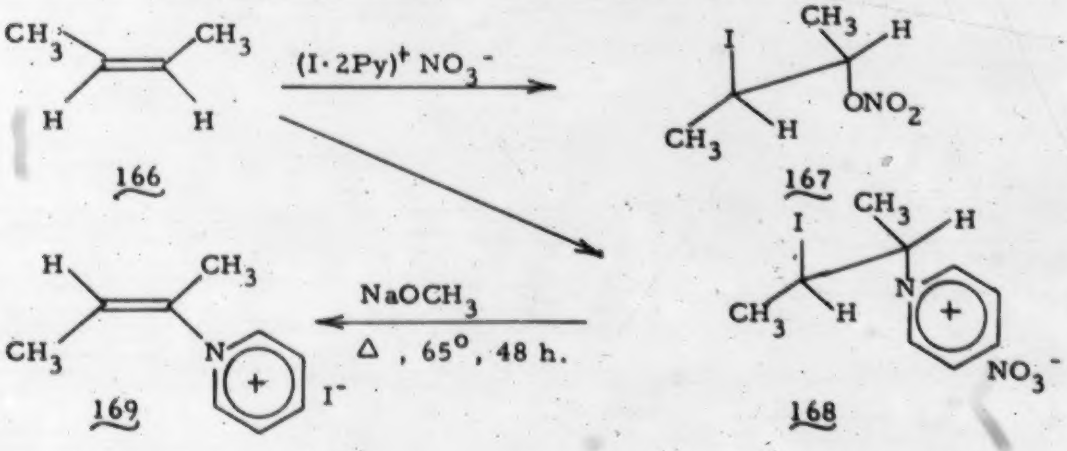

H
(CH3)3C
I
HO
CH3
H
136A
-HI
158


H
(CH3)3C
I
H3C
OH
H
159A
CH3
(CH3)3C
I
HO
H
H
159B
+
OH
(CH3)3C
I
H
CH3
H
159C
-HI
160
161

Thus the addition of iodonium nitrate to 4,4-dimethylpent-2-enes is stereospecific and regiospecific at least with regard to the iodonitrate esters. The iodopyridinium nitrate salts 137 and 157 although clearly epimers (n.m.r.) were produced in such low yields that it was inconvenient to ascertain the stereochemistry in this particular example. When the two but-2-enes were used the relative yields of the pyridinium salts were much higher reflecting the reduced steric hindrance during the addition and permitting an examaination of their stereochemistry.

(E)-But-2-ene 162 on reaction with iodonium nitrate in chloroform-pyridine produced the iodonitrate ester 163 and the iodoalkyl pyridinium nitrate 164 in 32% and 55% yields respectively, both stereoisomerically pure. The possibility that pyridinium salts such as 164 may arise from iodonitrate esters such as 163 by displacement of the nitrate by pyridine was discounted since 163 did not give any 164 under conditions in which 164 is formed even after 24 h. Treatment of 164 with sodium methoxide in methanol at 50° for 24 h afforded the single diastereomeric elimination product 165. Similar treatment of (Z)-but-2-ene 166 with iodonium nitrate produced the iodonitrate ester 167 and the corresponding iodopyridinium nitrate 168 stereospecifically in 32% and 54% yields respectively. Treatment of 168 with sodium methoxide in refluxing methanol for 48 h. gave the single diasteromeric


CH3
H
H
CH3
162
(I·2Py)+NO3-
H
CH3
I
ONO2
CH3
H
163
CH3
CH3
H
N
+
I-
165
NaOCH3, 24 hr.
50°
H
CH3
I
N
+
CH3
H
NO3-
164


CH3
CH3
H
H
166
(I·2Py)+ NO3-
I
CH3
H
ONO2
CH3
H
167
H
CH3
CH3
N
+
I-
169
NaOCH3
Δ, 65°, 48 h.
I
CH3
H
N
+
CH3
H
NO3-
168

elimination product **169**.

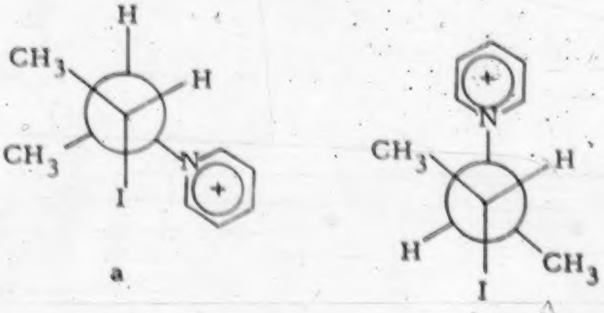
The configurational assignments of **165** and **169** were made by n.m.r. spectroscopy. It has been shown that in compounds of the type **170**, the two methyl groups can couple and the magnitude of this

$$CH_3-CH=CX-CH_3$$

170 X = Halogens, $COOCH_3$, N_3, etc.

homoallylic coupling constant depends on the relative configuration of the two methyl groups, the *trans*-methyl groups showing a larger coupling constant than the *cis*-methyl groups[181]. The methyl groups in compound **165** showed a coupling constant of 1.3 Hz while those in compound **169** showed a coupling constant of 1.7 Hz. Thus **165** and **169** have the *cis* and *trans* configurations respectively. Since base catalyzed eliminations proceed stereospecifically *trans*[182], the formation of **165** and **169** show that the iodoalkyl pyridinium nitrates, **164** and **168**, have the *erythro* and *threo* configurations respectively. It is also clear that the iodoalkyl nitrate esters and the iodoalkyl pyridinium nitrates arise from the same intermediate by nucleophilic attack by nitrate ion and pyridine respectively and that the products are formed under kinetic control and that they do not interconvert to any appreciable extent.

The marked difference in the relative ease of elimination of hydrogen iodide from iodopyridinium salts **164** and **168** can be accounted for from considerations of conformational analysis. Of the three staggered conformations to be considered for the *erythro* isomer **164**, conformer **164b** might be predicted to be the preferred conformation. However the rapid *trans* elimination of hydrogen iodide even



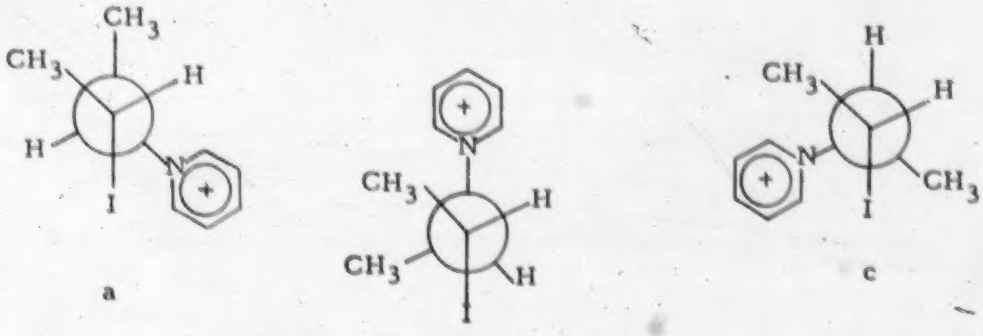
a b c

164

at room temperature suggests significant contribution from conformation 164a, implying a compensating attractive force between gauche iodo and pyridinium groups. The X-ray crystallographic study of N-[2-(2-methyl-3-iodo)butyl] pyridinium nitrate 28 shows the largest groups iodo and pyridinium to be similarly oriented gauche to one another[135].

Hassner has reported that London attractive forces between vicinal iodo and azide groups in iodine azide adducts similarly favor an adoption of gauche relative positions for these groups[2,183].

In the case of the *threo* isomer 168, the three conformers to be considered are 168a-c. For this isomer the most stable conformation should be 168a in accord with the observation that base catalyzed



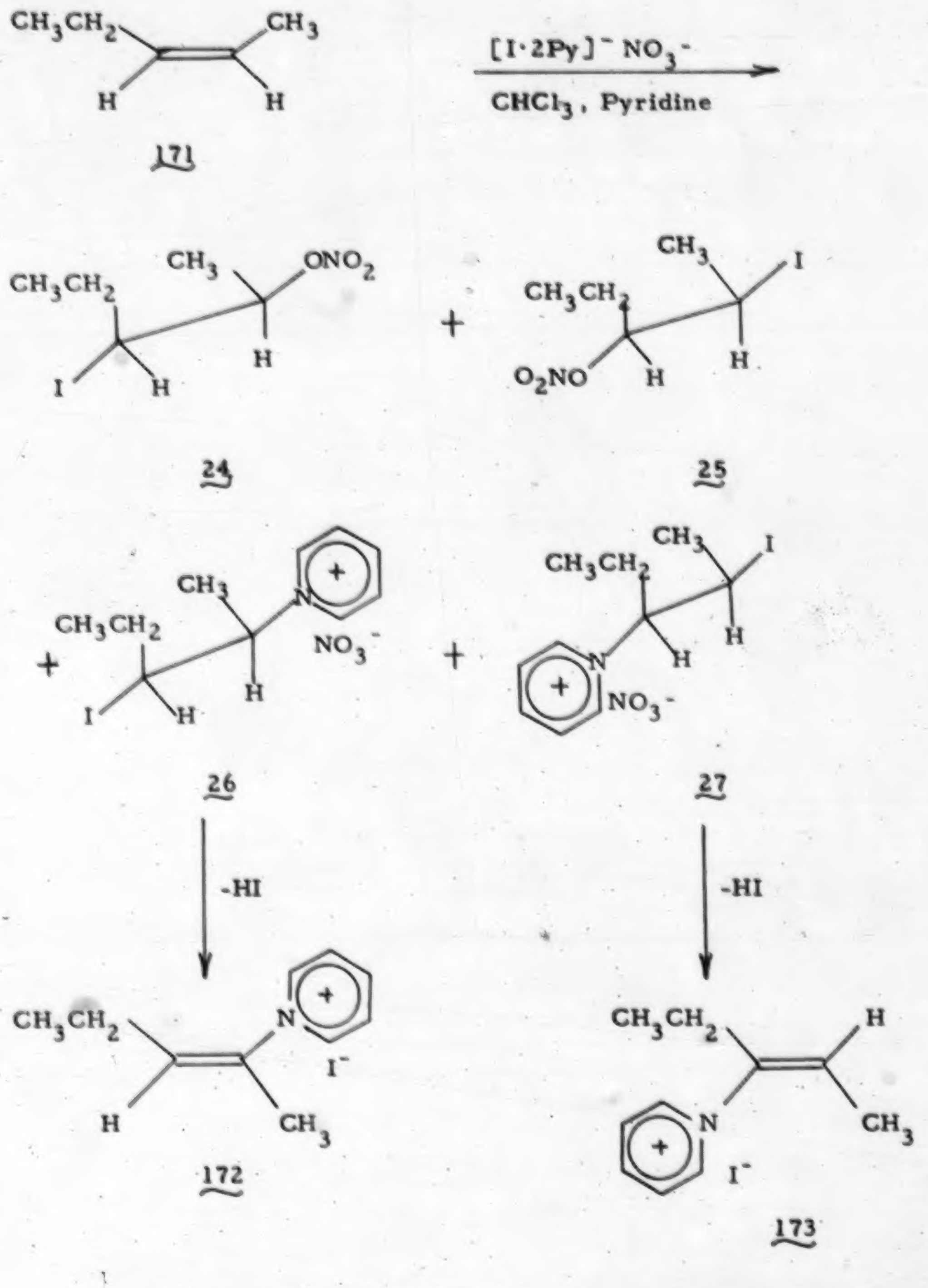
a b c

168

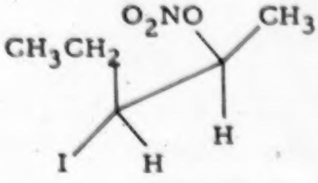
trans elimination of hydrogen iodide requires much more vigorous conditions than for 164 (i.e. sodium methoxide in refluxing methanol for 48 h) and is still incomplete. The attractive gauche iodo-pyridinium interaction in 168a may reinforce the conformational preference.

Addition of iodonium nitrate to (Z)-pent-2-ene 171 in chloroform-pyridine was regioselective in the formation of the *threo*-iodonitrates 24 and 25 in a ratio of 70:30 and in a combined yield of 67%. The isomer ratio was determined from the n.m.r. spectrum which showed $\delta_{\mathrm{TMS}\,(\mathrm{CDCl_3})}$: 4.1 (sextet, 0.7H) and 4.33 (octet, 0.3 H) corresponding to two iodomethine groups. The corresponding absorptions for the two nitrato-methine groups occured at δ5.15 (octet, 0.7H) and δ4.81 (quint, 0.3 H) respectively.

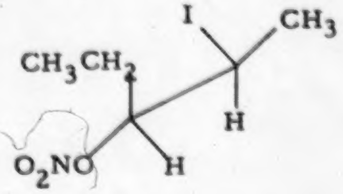
The *threo*-iodoalkyl pyridinium salts formed in the above reaction was a regio isomeric mixture of 26 and 27, with the anti-Markovnikov product 26 predominating in approximately the same ratio as for the iodonitrate esters. This was evident from the n.m.r. spectrum of the product which showed two partially superimposed triplets at $\delta_{\mathrm{TMS}\,[(\mathrm{CD_3})_2\mathrm{SO}]}$: 0.7-1.2, although the exact ratio could not be determined. The latter was determined by base catalyzed elimination of hydrogen iodide from the pyridinium salts 26 and 27 to the corresponding vinyl pyridinium salts 172 and 173. The isomer ratio was established by comparing the n.m.r. intensities of the vinyl methyl groups in 172 and 173, which absorbed at $\delta_{\mathrm{TMS}\,[(\mathrm{CD_3})_2\mathrm{SO}]}$: 2.34 as a singlet, further split by allylic and homoallylic coupling, and at δ1.42 as a doublet, further split by homoallylic coupling, respectively in a ratio of 73:27.


[I·2Py]⁻ NO₃⁻
CHCl₃, Pyridine
171
24
25
26
27
-HI
-HI
172
173

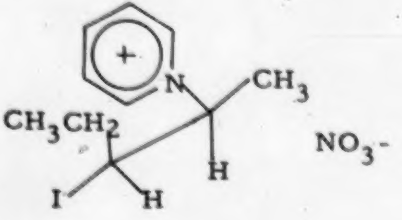
The corresponding reaction of iodonium nitrate in chloroform-pyridine with (E)-pent-2-ene 174 similarly afforded a mixture of regioisomeric iodonitrate esters 175 and 176 in a combined yield of 53% and in a ratio of 69:31 as determined by comparing the n.m.r. intensity of the methyl alpha to the nitrato-methine group in 175 with the total intensity of the methyl groups of the ethyl groups. The iodopyridinium salt formed in this reaction was a single regioisomer 177 as clearly shown by the n.m.r. spectrum.


O2NO
CH3
CH3CH2
I
H
H

175

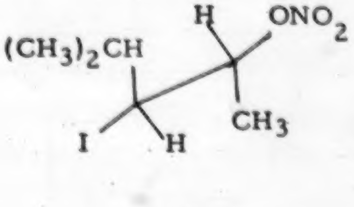

I
CH3
CH3CH2
H
O2NO
H

176

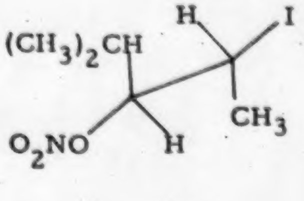

+
N
CH3
CH3CH2
NO3-
H
I
H

177

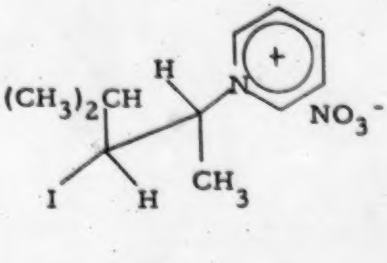
Electrophilic addition of iodonium nitrate to 4-methylpent-2-enes represents a borderline case in that addition to the (E)-isomer is 80% regioselective while addition to the (Z)-isomer is regiospecific in the formation of iodonitrate esters. The nucleophilic attack of the larger pyridine is regiospecific with both isomers as evidenced by the n.m.r. spectra. From the (E)-isomer 178 were obtained iodonitrate esters 179 and 180 in a combined yield of 70% and iodopyridinium nitrate 181 in a yield of 15%. The corresponding yields of the


H
ONO2
(CH3)2CH
CH3
I
H

179

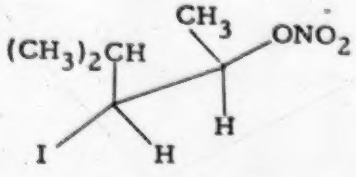

H
I
(CH3)2CH
CH3
O2NO
H

180

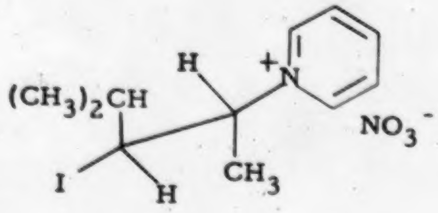

H
+
N
(CH3)2CH
NO3-
I
H
CH3

181

regiospecific iodonitrate ester **183** and the iodopyridinium nitrate **184** from the (Z)-isomer **182** were 63% and 14% respectively.

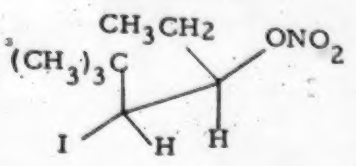

CH3
(CH3)2CH
ONO2
I
H
H

183

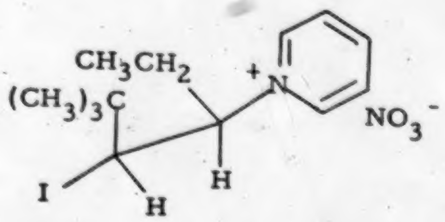

H
+N
(CH3)2CH
NO3-
I
H
CH3

184

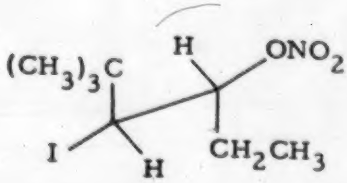
The greater steric bulk offered by the *tert*.-butyl group in 2,2-dimethylhex-3-enes ensures regiospecific anti-Markovnikov addition[1,184] producing the *threo* iodonitrate ester **186** in 80% yield from the (Z)-olefin **185** and the *erythro*-isomer **189** in 55% yield from the (E)-alkene **188**. Only traces of the corresponding iodopyridinium salts **187** and **190** were formed.


CH3CH2
(CH3)3C
ONO2
I
H
H

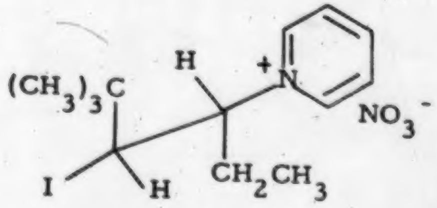
186


CH3CH2
(CH3)3C
+N
NO3-
I
H
H

187

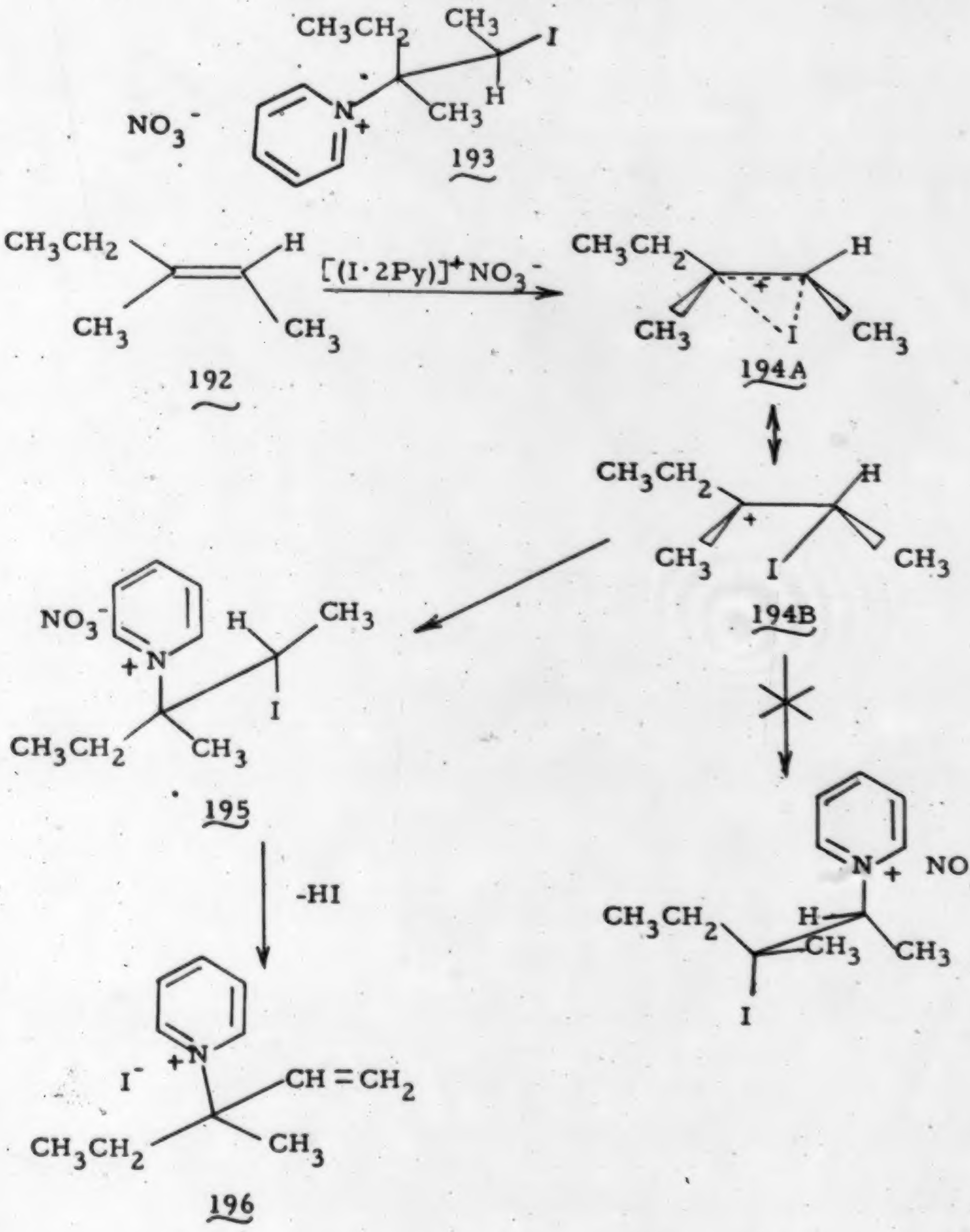

(CH3)3C
H
ONO2
I
H
CH2CH3

189


(CH3)3C
H
+N
NO3-
I
H
CH2CH3

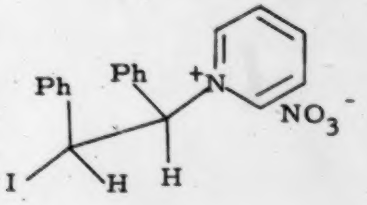
190

Addition of iodonium nitrate to (Z) and (E)-3-methylpent-2-enes 191 and 192, although they do not contain especially bulky groups, afforded exclusively the diastereomeric iodopyridinium nitrates 193 and 195 in regiospecific and stereospecific additions. The regiochemistry

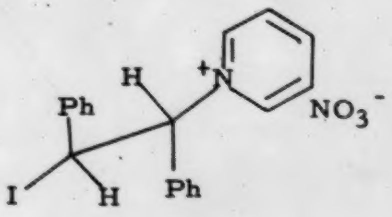

CH3CH2
CH3
I
H
NO3-
N+
CH3
193
CH3CH2
H
CH3
CH3
192
[(I·2Py)]+ NO3-
CH3CH2
H
+
CH3
I
CH3
194A
CH3CH2
H
+
CH3
I
CH3
194B
NO3-
+N
H
CH3
I
CH3CH2
CH3
195
-HI
N+
NO3-
CH3CH2
H
CH3
CH3
I
+N
I-
CH = CH2
CH3CH2
CH3
196

of the addition was proven by the sodium methoxide catalyzed elimination of hydrogen iodide from 195 to form 196 the n.m.r. spectrum of which showed a clear ABB' pattern for the vinyl protons.

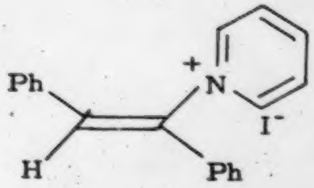
Addition of iodonium nitrate to (Z) and (E)-stilbenes, 197 and 198, to form the iodoalkyl pyridinium nitrates, 199 and 200, is also stereospecific. No iodonitrate esters were formed in these reactions. Base catalyzed trans-elimination of hydrogen iodide from 199 and 200 gave the isomeric vinyl pyridinium salts 201 and 202.



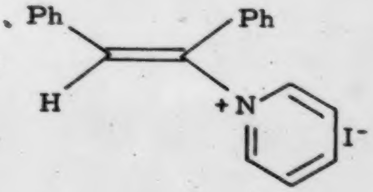
199



200

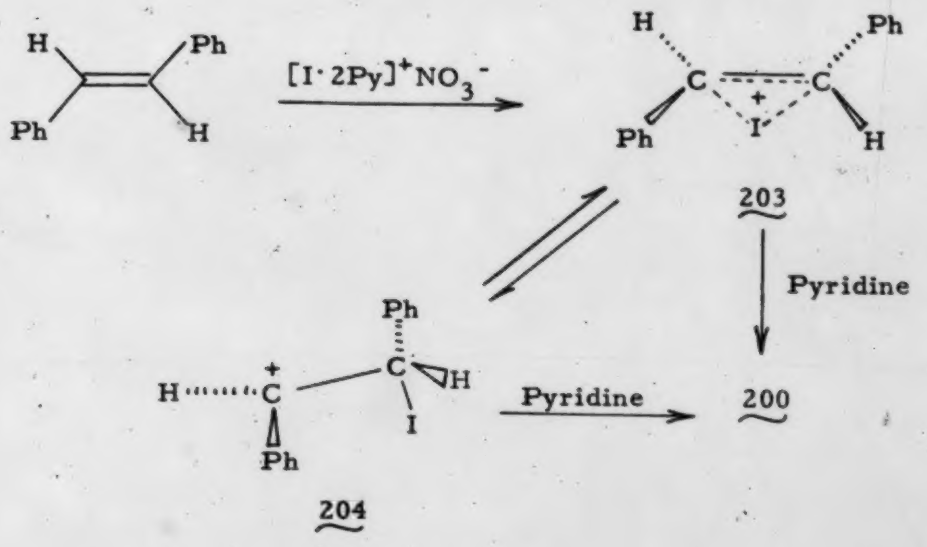


201

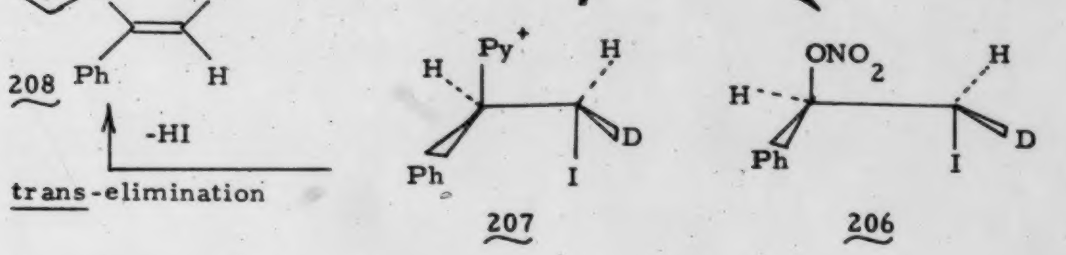


202

The trans stereospecificity observed in iodonium nitrate additions to (Z) and (E)-stilbenes and to (Z) and (E)-3-methylpent-2-enes can be explained as proceeding through an iodonium ion such as 203 for aryl substituted olefins. But it is also possible to attribute this specificity to hindrance of free rotation by the phenyl groups in an intermediate such as 204. To eliminate such a possibility an addition


[I·2Py]⁺NO₃⁻
203
Pyridine
204
Pyridine
200

to (Z)-2-deuterostyrene 205 was performed. Olefin 205 was prepared from phenylacetylene by deuteration and reduction with disiamylborane by the method reported by Hassner[104]. The styrene 205 contained >95% deuterium, as determined by n.m.r. and mass spectroscopy. As in the case of the protium analog the products were the iodonitrate ester 206 and a mixture of pyridinium salts 207 and 208, 208 arising from spontaneous trans-elimination of hydrogen iodide from 207. On


205
[(I·2Py)]⁺NO₃⁻
?
NO₃⁻
208
-HI
trans-elimination
207
206

treatment of the mixture of pyridinium salts with potassium carbonate 208 was produced. The structure of 208 follows from comparison of the n.m.r. spectrum (vinyl singlet at δ6.43) with that of the protium analog (vinyl AB quartet at δ6.43 and 6.10, J=2.5 Hz). In such compounds the proton cis to the phenyl absorbs at lower field than the trans proton[104].

Evidently, the iodonium ion implicated in iodonium nitrate additions, unlike that formed in other pseudohalogen additions[1,104,96], has sufficient free cation character, e.g. 194B, to permit nucleophilic attack despite increased steric hindrance and to permit neighboring hydroxyl group attack to form three, four, five and six membered cyclic ethers. It also has sufficient stability through the bridged form 194A to ensure its stereochemical integrity is maintained leading to the observed stereochemistry of formation of e.g. 195 and its diastereomer, and of 207. It appears therefore that the intermediate iodonium ion should be represented by the unsymmetrically bridged species 194A with contribution from the free cationic form 194B.

CHAPTER V

Kinetics and Energetics of the Addition of Iodonium Nitrate to Unsaturated Systems.

In Chapter III, we have seen that addition of iodonium nitrate in both chloroform-pyridine and chloroform-sym-collidine to suitable olefinic substrates gives cyclized and/or addition products depending upon the structure of the substrate. This result signifies neighboring group participation in contrast to the known chemistry of iodine isocyanate[96] and iodine azide[109]. Also, addition of iodonium nitrate to cyclohex-2-en-1-ol and cyclohept-2-en-1-ol gives products derived from intermediate iodonium ions which are formed cis to the hydroxyl group, signifying some compensating interaction between the iodine and hydroxyl group. On the other hand addition of iodonium nitrate to cyclooct-2-en-1-ol results in a product derived from an iodonium ion which is formed trans to the hydroxyl group indicating that steric hindrance by the hydroxyl group for the approach of the electrophile is the overriding factor. The results with these cyclic olefinic alcohols are in agreement with the observed stereochemistry of epoxidation of these compounds.

A comparison of the relative yields of iodonitrate esters and iodopyridinium salts for olefinic alcohols and alkenes of comparable structure (Table 3) reveals that in general introduction of a hydroxy function results in a marked increase in the proportion of the iodopyridinium salt relative to that of the iodonitrate. This suggests that the hydroxy function contributes to the increased stabilization of the intermediate iodonium ion rather than to its inductive destabilization.

Table 3

Substrate	Relative Yields Iodonitrates	 Pyridinium salts
C_2H_5-CH(OH)-CH_2-CH=CH_2	1 :	2.0
CH_2(OH)-CH_2-CH=CH_2	1 :	1.6
n-Bu-CH=CH_2	1 :	1.0
Cyclohex-2-en-1-ol	1 :	0.805
Cyclohexene	1 :	0.66
Cyclopent-2-en-1-ol	1 :	0.423
Cyclopentene	1 :	0.17
Cyclohept-2-en-1-ol	1 :	0.593
Cycloheptene	1 :	0.169
Cyclooct-2-en-1-ol	60%	-
Cyclooctene	1 :	0.0696

Iodonium nitrate like other typical pseudohalogens has all the characteristics of an electrophilic reagent which is consistent with the qualitative observation that electron donating groups facilitate the reaction while electron withdrawing groups considerably retard it or even arrest it. But iodonium nitrate differs from the other pseudohalogens in that in this reagent the iodine is complexed to two pyridine groups through nitrogen. The effect of this complexation may alter its relative electrophilicity compared to other iodine containing pseudohalogens such as iodine isocyanate, iodine chloride etc., depending upon the electronic and steric environments in the olefinic substrate.

We undertook an extensive kinetic study of the addition of iodonium nitrate to olefins of varying nucleophilic character with a view to obtaining evidence for neighboring group participation and thermodynamic parameters.

Estimation of Iodonium Nitrate.

As in the case of other positive halogen containing compounds, iodonium nitrate can be estimated by the iodometric method. But unfortunately we could not make use of this method for kinetic purposes since many of the adducts easily generate iodine with potassium iodide in the presence of acetic acid.

Swern and coworkers used the gas chromatographic method to follow the disappearance of olefin in the addition of iodine isocyanate[99]. This method was not applicable for iodonium nitrate additions since the reaction mixture contains soluble nonvolatile iodoalkyl pyridinium salts.

Attempts to follow the kinetics by studying the rate of formation of the products by means of high pressure liquid chromatography were not successful. It was found that the products can be detected (after destroying the iodonium nitrate with sodium thiosulfate and then drying the solution with molecular sieves), but it requires a solvent of low polarity such as hexane. Under these conditions the unreacted olefin eluted with chloroform. But the iodopyridinium salt remained on the column, thus building up the pressure. Elution of the pyridinium salt requires a solvent of high polarity such as acetonitrile and methanol. Again no quantitative correlation was found.

Since positive halogens can be reduced with sodium thiosulfate or sodium bisulfite, we examined the applicability of this method for the estimation of iodonium nitrate. We found that iodonium nitrate can be estimated quantitatively with thiosulfate. This gave values comparable with those obtained by the iodometric method. The probable reaction may be formulated as:

$$2\,Na_2S_2O_3 + INO_3 \longrightarrow NaI + NaNO_3 + Na_2S_4O_6$$

The method is as follows:

A known volume of iodonium nitrate solution in chloroform-pyridine (70:30) is thoroughly shaken with an excess of a known volume of standard sodium thiosulfate solution. The completion of the reaction between sodium thiosulfate and iodonium nitrate is indicated by the change in color of the iodonium nitrate solution from light yellow to colorless (ca. 15-20 sec.). The excess of sodium thiosulfate is then determined by titration with standard iodine solution using starch as the indicator. The titre values were quite reproduceable within experimental limits. The end point is indicated by the first appearance of the blue color. It was found that the color faded gradually.

In some additions, where cyclization (e.g. pent-4-en-1-ol, hex-5-en-1-ol) or rearrangement (e.g. norbornylene) occurs, pyridinium nitrate ($Py \cdot HNO_3$) is an additional product in the reaction. To perform kinetic measurements on such compounds, it was necessary to determine whether the pyridinium nitrate will interfere with the estimation of iodonium nitrate by the method described above. It was found that the titre values were unchanged in the presence of added pyridinium nitrate.

Preparation of Iodonium Nitrate-Pyridine Complex for Kinetic Studies.

A solution of iodonium nitrate in chloroform-pyridine was prepared in the usual way (see experimental section). The solution was poured into an excess of anhydrous ether with stirring. The precipitated solid was collected and washed several times with ether. The product was recrystallized several times from anhydrous acetonitrile or acetonitrile-ether. It was not possible to remove all silver salts from the complex because of their solubility in acetonitrile. An approximate purity of 95% was achieved by this method.

The presence of silver salts was shown not to interfere with the reaction by studying kinetics with samples of complex containing different amounts of silver salts.

Stoichiometry of the Reaction.

The stoichiometry of the reaction was shown to be 1:1 by allowing a known excess of iodonium nitrate in chloroform-pyridine to react with a known amount of cyclohexene to completion and then determining the excess of iodonium nitrate by the method described above.

Kinetic Measurements.

All kinetic studies were done in chloroform-pyridine (70:30 v/v) at temperatures between -20.5 to 45°C. Chloroform and pyridine were freshly distilled. All olefinic substrates were fractionally distilled before use. Purities were determined by gas chromatographic studies.

The progress of the reaction was followed by the rate of disappearance of iodonium nitrate. An accurately weighed amount of olefin was made up to 50 ml with chloroform-pyridine (70:30) at the temperature at which kinetic measurements were made. The olefin solution and the iodonium nitrate solution (50 ml) were equilibrated at the desired temperature. The two solutions were mixed thoroughly. 5 ml portions of the reaction mixture were withdrawn at intervals and the unreacted iodonium nitrate was estimated by the method described before. Whenever possible the kinetics were followed up to 80-85% of the reaction except at very low temperatures where they were followed up to 50-60%.

In all the kinetic runs a slight excess (10-25%) of iodonium nitrate was used. The initial concentration of iodonium nitrate was determined by titrating 5 ml of the stock solution. This was checked by titrating a sample after completion of the reaction. Good agreement was observed within experimental error.

A typical kinetic run may be represented as follows:

Time (min.)	5	10	20	30	40	50	60	80	100	120
$I_2 \equiv$ excess thiosulfate(mls)	1.3	2.85	5.45	7.8	9.9	11.9	13.6	16.4	18.8	20.7

From the data the concentration of iodonium nitrate at any time can be calculated. Since the difference in the initial concentrations of iodonium nitrate and olefin is known, the concentration of olefin at any time follows.

Determination of Rate Constants.

The second order rate constants for the addition of iodonium nitrate to various olefinic substrates were determined by plotting log P against time.

$$P = \frac{c_b^o \cdot c_a}{c_a^o \cdot c_b}, \text{ where}$$

c_a^o = initial concentration of iodonium nitrate

c_b^o = initial concentration of olefin

c_a and c_b are concentrations of iodonium nitrate and olefin respectively at any given time.

Good second order plots (straight lines) were obtained up to about 80-85% of the reaction.

$$k = \text{Slope} \cdot \frac{2.303}{c_a^o - c_b^o}$$

Results and Discussion.

Figures 2 and 3 represent selected typical standard and weighted least squares plots for the determination of second order rate constants for the addition of iodonium nitrate to various olefins.

The second order rate constants at 0°C for the reaction of iodonium nitrate with a few cyclic olefins and the corresponding olefinic alcohols (hydroxy group on the α-carbon atom) along with their concentrations are given in Table 4. For the monocyclic olefins the order of increasing rate of reaction is cyclooctene $<$ cycloheptene $<$ cyclohexene $<$ cyclopentene. Norbornadiene is approximately 2.5 times as reactive as norbornylene towards iodonium nitrate. Although norbornadiene may be expected to be twice as reactive as norbornylene for statistical reasons, the overall enhancement of rate by 2.5 times may be attributed to neighboring π bond participation.

The effect of an α- hydroxy group in the monocyclic olefinic systems on the rate of reaction is also evident. In the five, six and

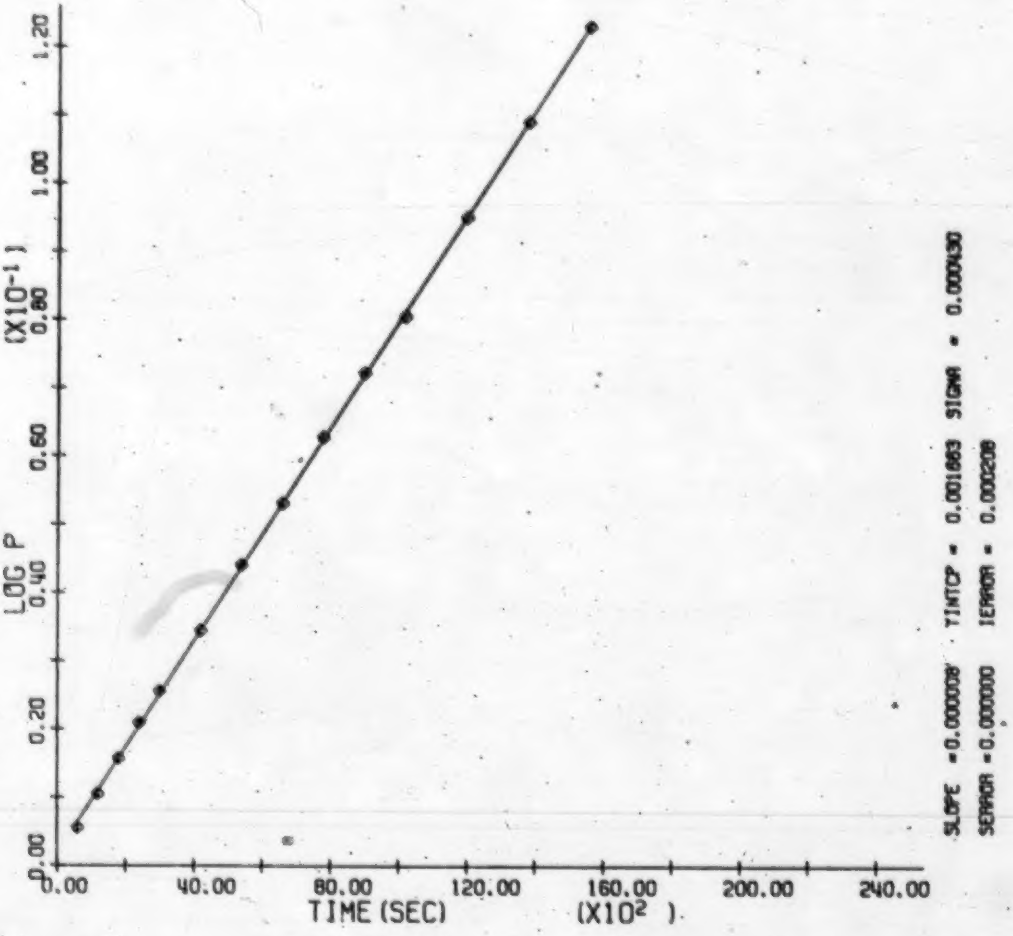
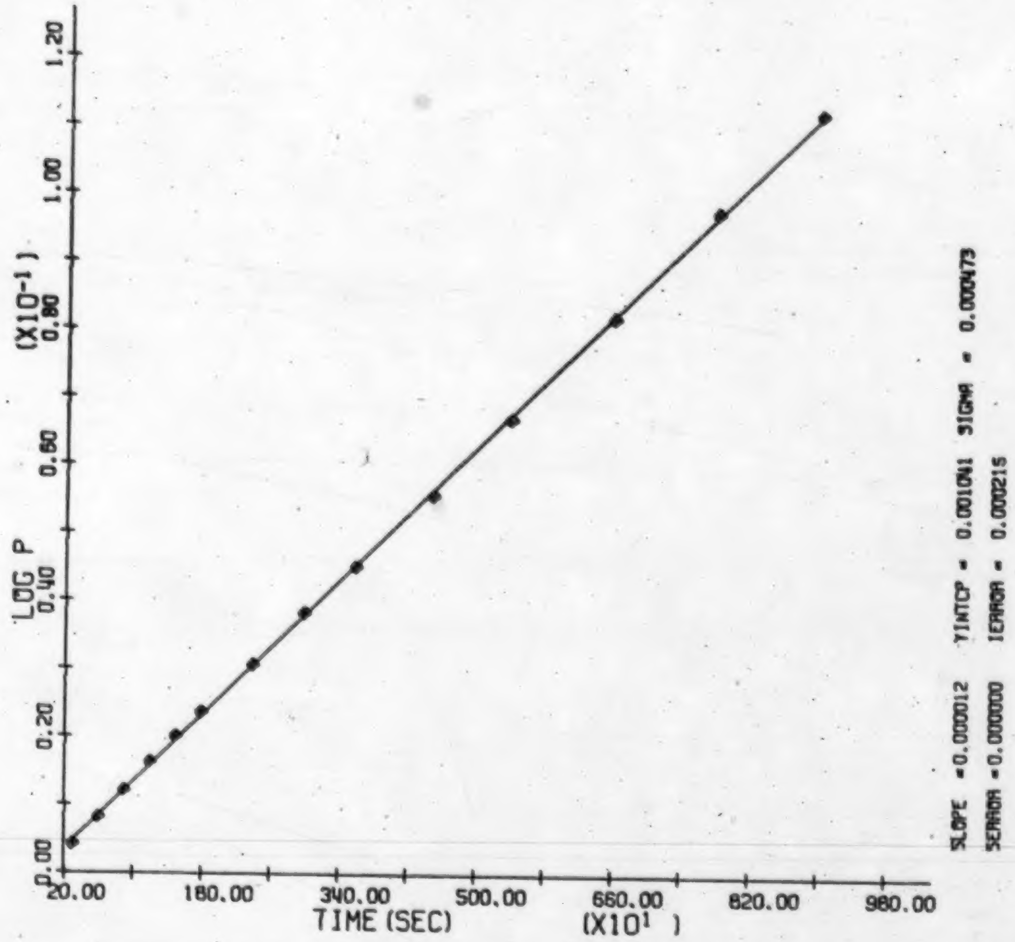


Figure 2. Plot of log P against time (sec.) for the addition of iodonium nitrate to cycloheptene at -11.5°C in 70% chloroform and 30% pyridine.



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SERROR =0.0000000  IERROR = 0.0000215
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Figure 3. Plot of log P against time (sec.) for the addition of iodonium nitrate to cyclooct-2-en-1-ol at 37°C in 70% chloroform and 30% pyridine.

Table 4

Second Order Rate Constants, k (liter mole^{-1} sec^{-1}) for the Addition of Iodonium Nitrate at 0°C in 70% Chloroform and 30% Pyridine.

Substrate	Conc. of Iodonium Nitrate (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
Cyclopentene	0.04785	0.04258	$7.958 \pm 0.063 \times 10^{-3}$
Cyclopent-2-en-1-ol	0.02786	0.02322	$1.115 \pm 0.008 \times 10^{-2}$
Cyclohexene	0.07770	0.04897	$7.078 \pm 0.115 \times 10^{-3}$
Cyclohex-2-en-1-ol	0.04462	0.04054	$1.169 \pm 0.011 \times 10^{-2}$
Cycloheptene	0.04184	0.04102	$4.241 \pm 0.039 \times 10^{-3}$
Cyclohept-2-en-1-ol	0.04929	0.03937	$9.501 \pm 0.27 \times 10^{-3}$
Cyclooctene	-	-	3.365×10^{-4}*
Cyclooct-2-en-1-ol	-	-	2.213×10^{-5}*
Norbornylene	0.04785	0.04407	$3.24 \pm 0.063 \times 10^{-3}$
Norbornadiene	0.05003	0.03986	$8.141 \pm 0.068 \times 10^{-3}$

* Obtained by extrapolation to 0°C.

seven membered cyclic systems, the alcohols are more reactive than the corresponding olefins. Thus cyclohex-2-en-1-ol is 1.5 times as reactive as cyclohexene, cyclohept-2-en-1-ol 2.25 times as reactive as cycloheptene, and cyclopent-2-en-1-ol 1.4 times as reactive as cyclopentene. Since in cyclohex-2-en-1-ol the iodonium ion is formed *cis* to the hydroxy group whereas in cyclohexene both sides of the unsaturated centre are available for electrophilic attack, the above result indicates a rate enhancement by a factor of three in spite of the inductive electron withdrawal by the hydroxy group. On the same grounds the rate enhancement for cyclohept-2-en-1-ol by a factor of 4.5 compared to cycloheptene indicates that the major reaction pathway for this particular olefinic alcohol is through an intermediate iodonium ion which is formed *cis* to the hydroxy group. Similarly a rate enhancement by a factor of 2.8 for cyclopent-2-en-1-ol compared to cyclopentene and the fact that cyclopent-2-en-1-ol gives only one diastereomeric iodonitrate ester and iodopyridinium nitrate suggest that the iodonium ion may be formed *cis* to the hydroxy group.

The rate constants for cyclooctene and cyclooct-2-en-1-ol show that the hydroxy group has the opposite effect on the reaction rate. This may indicate that steric hindrance and/or inductive electron withdrawal by the hydroxy group to the approach of the electrophile are the overriding factors and that the iodonium ion may be formed *trans* to the hydroxy group.

Table 5 summarizes the second order rate constants at 0° for a few linear olefinic alcohols of varying chain lengths and substitution pattern. The value for hex-1-ene is included for comparison, since there is expected to be very little variation in rate constants

Table 5

Second Order Rate Constants, k (liter $mole^{-1}$ sec^{-1}) for the Addition of Iodonium Nitrate at 0°C in 70% Chloroform and 30% Pyridine.

Substrate	Conc. of Iodonium Nitrate (mole $liter^{-1}$)	Conc. of Olefin (mole $liter^{-1}$)	k
Hex-1-ene	0.05635	0.05014	$3.089 \pm 0.028 \times 10^{-3}$
Allyl alcohol	0.07770	0.04735	$9.042 \pm 0.17 \times 10^{-3}$
But-3-en-1-ol	0.02226	0.02099	$7.439 \pm 0.058 \times 10^{-3}$
Pent-4-en-1-ol	0.02226	0.01742	$3.979 \pm 0.025 \times 10^{-3}$
Hex-5-en-1-ol	0.0535	0.04510	$2.829 \pm 0.032 \times 10^{-3}$
Z-Hex-3-en-1-ol	0.02465	0.01953	$4.182 \pm 0.053 \times 10^{-2}$
Hex-1-en-3-ol	0.02465	0.01881	$7.714 \pm 0.14 \times 10^{-3}$
3-Methylbut-3-en-1-ol	0.02465	0.02139	$3.950 \pm 0.101 \times 10^{-2}$
3,3-Dimethylbut-1-ene	0.1244	0.1075	$1.118 \pm 0.028 \times 10^{-3}$

along the series propene to hex-1-ene in electrophilic addition reactions[147].

The order of decreasing reactivity for the linear unsubstituted olefinic alcohols is allyl alcohol > but-3-en-1-ol > pent-4-en-1-ol > hex-5-en-1-ol. The rate constant for hex-5-en-1-ol is comparable with that for hex-1-ene indicating that the hydroxy group does not have any profound influence on the reaction rate when it is far removed from the reaction centre. The rate constants for the other three olefinic alcohols show that the stabilization of the intermediate iodonium ion by the hydroxy group is maximum when it is alpha to the olefinic centre and that the effect decreases as the distance between the hydroxy group and the olefinic center increases.

Comparison of the rate constants for allyl alcohol and hex-1-en-3-ol shows that introduction of an alkyl group on the hydroxy bearing carbon atom does not have any significant effect on the reaction rate. The small decrease in rate for hex-1-en-3-ol may signify steric hindrance by the alkyl group to the approach of the electrophile. This steric hindrance by alkyl groups is more pronounced in 3,3-dimethyl but-1-ene which is less reactive than hex-1-ene.

The facilitating effect on the reaction rate by alkyl substitutents on the olefinic carbon atom is evident from a comparison of the rate constant for but-3-en-1-ol with those for Z-hex-3-en-1-ol and 3-methylbut-3-en-1-ol. Substitution of one hydrogen of the terminal olefinic carbon atom in but-3-en-1-ol with an ethyl group results in a 5.6-fold increase in the reaction rate. A similar (5.3-fold) enhancement is also observed when the non-terminal olefinic carbon atom carries a methyl group as in 3-methylbut-3-en-1-ol.

The above kinetic studies show that in monocyclic monoolefin systems, introduction of a hydroxy group on the carbon atom alpha to the olefinic center results in a rate enhancement if the iodonium ion is formed cis to the hydroxy group as in cyclohexenol and cycloheptenol and in a decrease in rate if the iodonium ion is formed trans to the hydroxy group as seems to be the case for cyclooctenol. Also, in the case of olefinic alcohols of the type $CH_2=CH_2-(CH_2)_n-OH$, the rate decreases as n increases whereas for bromination in methanol, water, acetic acid and trifluoroacetic acid and for iodination in water the reverse has been observed[137b,147]. The drastically reduced extent of hydroxy participation for bromination in trifluoroacetic acid solvent has been attributed to hydrogen bonding between the solvent and the hydroxy substitutent which reduces it nucleophilicity and hence its effectiveness as a neighboring group[147]. The results for addition of bromine, iodine and iodonium nitrate are summarized in Table 6. Therefore it was of interest to determine the Arrhenius parameters for the addition of iodonium nitrate to the above olefinic alcohols to examine energetic and entropic effects on the additions.

The second order rate constants for the addition of iodonium nitrate in 70% chloroform and 30% pyridine to various olefins and olefinic alcohols are summarized in Tables 7-15. The increase in reaction rate with increasing temperature is evident from the tables. Although cyclohept-2-en-1-ol is less reactive than cyclohex-2-en-1-ol at 0°C and below, cross-over takes place at about 10°C.

Table 6 ;

Rate Coefficients for the Addition of Halogens and Iodonium Nitrate to Olefinic Alcohols , k (liter mole^{-1} min^{-1}).

Olefin	Bromination				Iodination	Iodonium Nitrate Addition at 0°C
	CH_3OH	H_2O (0.02M NaBr)	CH_3COOH (0.2M NaBr)	CF_3COOH (0.1M NaBr)	(H_2O, 0.0167M KI)	
$CH_2{=}CH{-}CH_2OH$	284 ± 4	1.36×10^7	251	3480	0.011 ± 0.0005	0.5425 ± 0.0102
$CH_2{=}CH{-}(CH_2)_2OH$	525 ± 4	$6.9 \pm 0.2 \times 10^7$	594	17000	0.023 ± 0.001	0.4463 ± 0.0035
$CH_2{=}CH{-}(CH_2)_3OH$	2630 ± 50	$31 \pm 1.4 \times 10^7$	4020	38900	2.2 ± 0.1	0.2387 ± 0.0015
$CH_2{=}CH{-}(CH_2)_4OH$	1730 ± 30	$37 \pm 1.5 \times 10^7$	1595	51500	0.38 ± 0.02	0.1697 ± 0.0019
$CH_2{=}CH{-}(CH_2)_4H$	2090	-	1730	101000	-	0.1854 ± 0.0017

Table 7

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cyclohexene in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (°C)	Conc. of $[I \cdot 2Py]^+ NO_3^-$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
-20	0.06760	0.05021	$5.153 \pm 0.077 \times 10^{-4}$
-13	0.06250	0.05028	$1.132 \pm 0.005 \times 10^{-3}$
0	0.07770	0.04897	$7.078 \pm 0.115 \times 10^{-3}$
14.5	0.01650	0.01539	$2.415 \pm 0.02 \times 10^{-2}$
23	0.01765	0.01529	$6.452 \pm 0.111 \times 10^{-2}$

Table 8

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cyclohex-2-en-1-ol in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (°C)	Conc. of $[I \cdot 2Py]^+ NO_3^-$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
-20	0.05130	0.04819	$9.636 \pm 0.11 \times 10^{-4}$
-11.5	0.06250	0.04085	$2.014 \pm 0.029 \times 10^{-3}$
0	0.04462	0.04054	$1.169 \pm 0.011 \times 10^{-2}$
14.7	0.01650	0.01461	$3.736 \pm 0.086 \times 10^{-2}$

Table 9

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cycloheptene in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (^{o}C)	Conc. of $[I\cdot 2Py]^{+} NO_3^{-}$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
-20	0.06760	0.05595	$4.047 \pm 0.044 \times 10^{-4}$
-11.5	0.06690	0.05270	$1.263 \pm 0.041 \times 10^{-3}$
0	0.04184	0.04102	$4.241 \pm 0.039 \times 10^{-3}$
23	0.01765	0.01551	$3.386 \pm 0.07 \times 10^{-2}$

Table 10

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cyclohept-2-en-1-ol in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (^{o}C)	Conc. of $[I\cdot 2Py]^{+} NO_3^{-}$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
-20	0.05130	0.04556	$7.295 \pm 0.065 \times 10^{-4}$
-13	0.06250	0.05098	$1.823 \pm 0.012 \times 10^{-3}$
0	0.04929	0.03937	$9.501 \pm 0.27 \times 10^{-3}$
15.1	0.01650	0.01358	$5.559 \pm 0.096 \times 10^{-2}$

Table 11

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cyclooctene in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (°C)	Conc. of $[I \cdot 2Py]^+ NO_3^-$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
22	0.05260	0.04742	$3.912 \pm 0.015 \times 10^{-3}$
28.3	0.03509	0.02985	$6.680 \pm 0.06 \times 10^{-3}$
35.1	0.02106	0.01873	$1.462 \pm 0.019 \times 10^{-2}$
42.2	0.01983	0.01688	$2.525 \pm 0.054 \times 10^{-2}$

Table 12

Second Order Rate Constants for the Addition of Iodonium Nitrate to Cyclooct-2-en-1-ol in 70% Chloroform and 30% Pyridine, k (liter mole^{-1} sec^{-1}).

Temperature (°C)	Conc. of $[I \cdot 2Py]^+ NO_3^-$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
22	0.07890	0.07070	$3.811 \pm 0.066 \times 10^{-4}$
30.3	0.05975	0.05098	$1.199 \pm 0.069 \times 10^{-3}$
37	0.04992	0.03761	$2.300 \pm 0.009 \times 10^{-3}$
45	0.04819	0.03829	$5.463 \pm 0.02 \times 10^{-3}$

Table 13

Second Order Rate Constants for the Addition of Iodonium Nitrate to Allyl Alcohol in 70% Chloroform and 30% Pyridine, k (liter $mole^{-1}$ sec^{-1}).

Temperature (^{o}C)	Conc. of $[I \cdot 2Py]^{+}NO_3^{-}$ (mole $liter^{-1}$)	Conc. of Olefin (mole $liter^{-1}$)	k
-20.5	0.05115	0.04067	$1.097 \pm 0.012 \times 10^{-3}$
-12	0.04436	0.04053	$3.020 \pm 0.035 \times 10^{-3}$
0	0.07770	0.04735	$9.042 \pm 0.17 \times 10^{-3}$
14.7	0.02226	0.01744	$4.826 \pm 0.041 \times 10^{-2}$

Table 14

Second Order Rate Constants for the Addition of Iodonium Nitrate to But-3-en-1-ol in 70% Chloroform and 30% Pyridine, k (liter $mole^{-1}$ sec^{-1}).

Temperature (^{o}C)	Conc. of $[I \cdot 2Py]^{+}NO_3^{-}$ (mole $liter^{-1}$)	Conc. of Olefin (mole $liter^{-1}$)	k
-20.5	0.05115	0.04035	$6.673 \pm 0.07 \times 10^{-4}$
-12	0.04450	0.04136	$1.685 \pm 0.016 \times 10^{-3}$
0	0.02226	0.02099	$7.439 \pm 0.058 \times 10^{-3}$
14	0.02226	0.01914	$2.638 \pm 0.019 \times 10^{-2}$

Table 15

Second Order Rate Constants for the Addition of Iodonium Nitrate to Pent-4-en-1-ol in 70% Chloroform and 30% Pyridine, k (liter mole^{-1}sec^{-1}).

Temperature (^{o}C)	Conc. of $[I \cdot 2Py]^{+} NO_3^{-}$ (mole liter^{-1})	Conc. of Olefin (mole liter^{-1})	k
-20.5	0.05145	0.04059	$3.393 \pm 0.045 \times 10^{-4}$
-13.5	0.05080	0.04052	$7.573 \pm 0.05 \times 10^{-4}$
0	0.02226	0.01742	$3.979 \pm 0.025 \times 10^{-3}$
14.3	0.02302	0.01697	$2.067 \pm 0.02 \times 10^{-2}$

For the determination of activation parameters, both log k and log$\frac{k}{T}$ were plotted against $\frac{1}{T}$. This gave good Arrhenius-type plots. Representative examples of standard and weighted least squares plot are given in Figures 4 and 5.

Table 16 summarizes the calculated activation parameters for the addition of iodonium nitrate to various olefins and olefinic alcohols. The E_a and $\Delta H^{\ddagger}$ values agree closely with those obtained by Kharasch and Orr[185] for the addition of 2,4-dinitrobenzenesulfenyl chloride to various para-substituted styrenes in acetic acid, whereas they are larger than those obtained for the addition of bromine in acetic acid to various para-substituted styrenes[186]. The E_a values are also larger than those for the addition of iodine in hexane to cyclohexene (5.3 Kcal mole^{-1}) and for the addition of iodine monobromide to

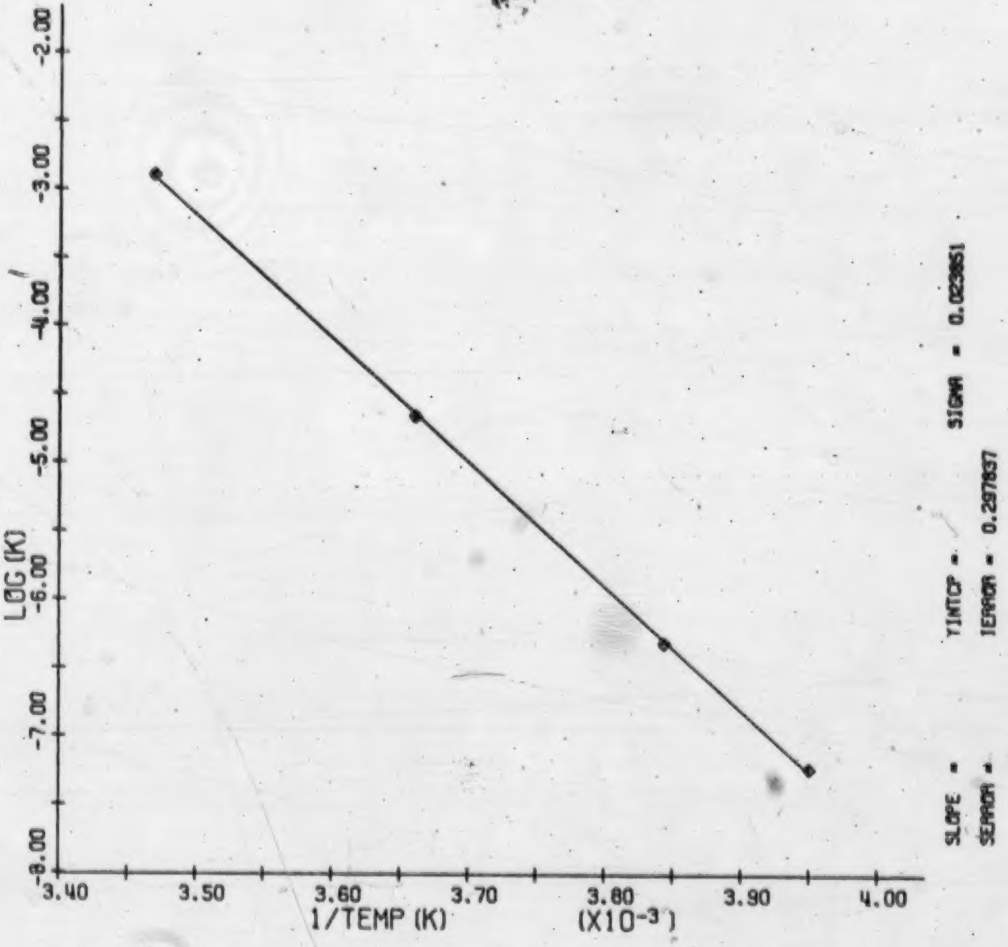


Figure 4. Plot of log k against 1/T for the addition of iodonium nitrate to cyclohept-2-en-1-ol in 70% chloroform and 30% pyridine.

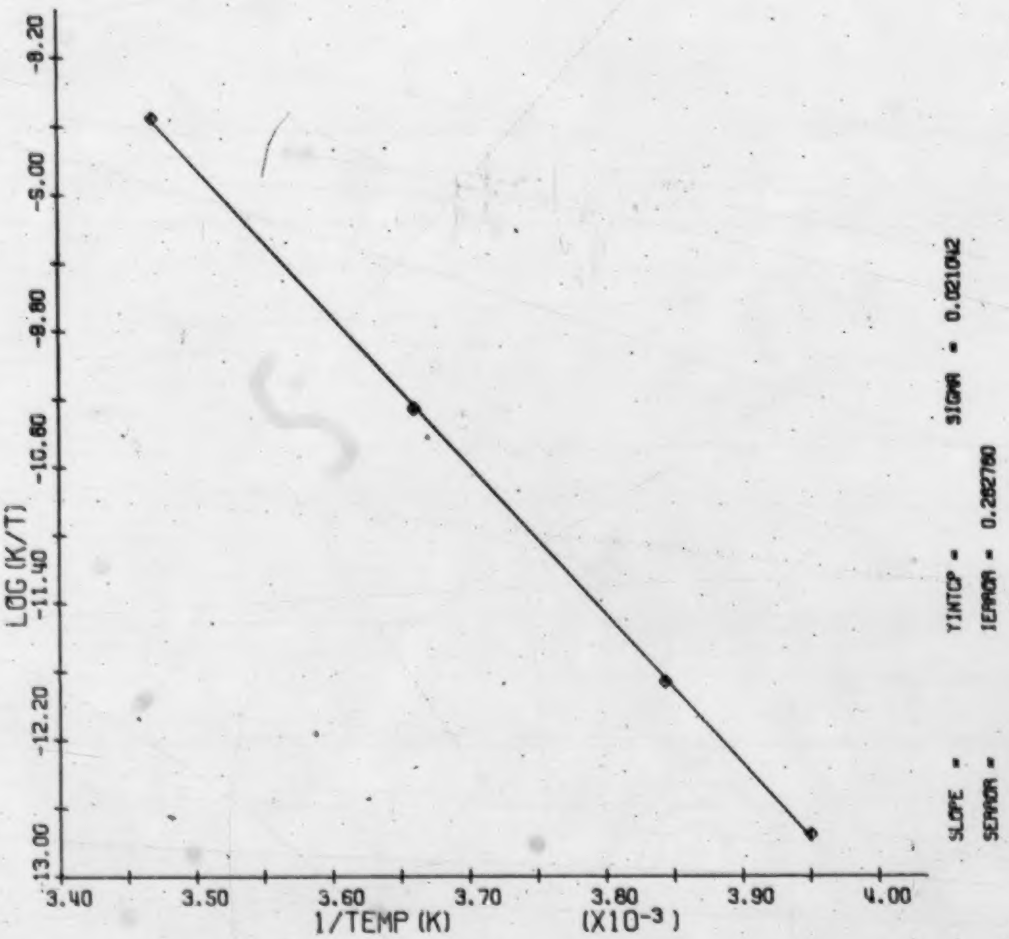


Figure 5. Plot of log k/T against 1/T for the addition of iodonium nitrate to cyclohept-2-en-1-ol in 70% chloroform and 30% pyridine.

Table 16

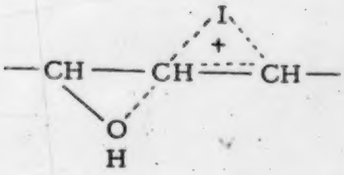
Activation Parameters for the Addition of Iodonium Nitrate in 70% Chloroform and 30% Pyridine.

Substrate	E_a (Kcal mole^{-1})	$\Delta S^{\ddagger}$ (entropy units)	$\Delta H^{\ddagger}$ (Kcal mole^{-1})
Cyclohexene	16.89 ± 0.6	- 9.554 ± 0.566	16.13 ± 0.61
Cyclohex-2-en-1-ol	15.92 ± 1.39	- 8.486 ± 1.075	16.19 ± 1.3
Cycloheptene	15.20 ± 0.42	-16.01 ± 1.033	14.56 ± 0.54
Cyclohept-2-en-1-ol	17.93 ± 0.16	- 3.877 ± 0.047	17.40 ± 0.14
Cyclooctene	17.52 ± 0.89	-12.45 ± 1.045	16.87 ± 0.89
Cyclooct-2-en-1-ol	21.36 ± 0.9	- 3.684 ± 0.25	20.82 ± 0.89
Allyl Alcohol	15.31 ± 0.7	-13.34 ± 1.03	14.78 ± 0.7
But-3-en-1-ol	15.60 ± 0.49	-13.15 ± 0.71	15.07 ± 0.49
Pent-4-en-1-ol	17.14 ± 0.38	- 8.48 ± 0.30	16.61 ± 0.36

cyclohexene in carbon tetrachloride (8.2 Kcal mole^{-1})[187]. On the other hand the $\Delta S^{\ddagger}$ values are comparatively low for the addition of iodonium nitrate than for the addition of sulfenyl chloride or bromine. This may indicate that in this bimolecular reaction, there is no large increase in polarity in the transition state compared to the reactants. This is not unexpected since the reacting pseudohalogen itself is considerably polarized as $[I \cdot 2Py]^{+}NO_3^{-}$.

The E_a and $\Delta H^{\ddagger}$ values for the six and seven membered cycloalkenes and the corresponding alcohols are similar. But it is apparent from the values for cycloheptene and cyclohept-2-en-1-ol that the alcohol requires higher activation energy and heat of activation for it to react with iodonium nitrate. This is more pronounced in cyclooctene and cyclooct-2-en-1-ol; the latter requires a much higher energy and heat of activation. The $\Delta S^{\ddagger}$ values also lead to the same conclusion. The small negative values of $\Delta S^{\ddagger}$ for the alcohols compared to those for the corresponding olefins may suggest that the transition state can be reached only with difficulty.

For the linear olefinic alcohols the E_a and $\Delta H^{\ddagger}$ values increase steadily from allyl alcohol to pent-4-en-1-ol whereas the $\Delta S^{\ddagger}$ values show a tendency to become less negative. This may suggest that the transition state for allyl alcohol is more favored both energetically and entropically than those for its higher homologues. This signifies considerable stabilization of the intermediate iodonium ion by the neighboring hydroxy group. This enhanced stabilization afforded the iodonium ion by the hydroxy group can be envisaged in a number of ways; participation to carbon **209**, participation to iodine **210**, or participation to the slightly positively charged pyridine nitrogen which may be still attached to the iodine in the transition state 211.



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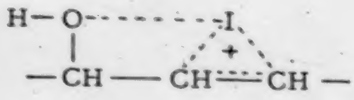

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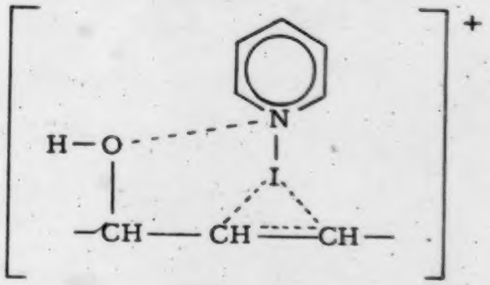
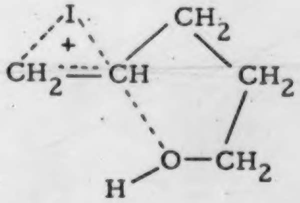


211

Since no such interaction to carbon or halogen has been observed in the iodination and bromination of allyl alcohol^{137b}, the participation may be to the nitrogen as in 211.

It was also observed that pent-4-en-1-ol with iodonium nitrate gives a substantial amount of cyclized product. Hex-5-en-1-ol behaved similarly, although to a lesser extent. This result signifies considerable participation to the carbon by the hydroxy group in the transition state, 212. So it is reasonable to assume that in allyl



212

alcohol and but-3-en-1-ol, the hydroxy group stabilizes the iodonium ion by participation to nitrogen, whereas in pent-4-en-1-ol and hex-5-en-1-ol, the stabilization is by participation to carbon. In the latter two compounds participation to nitrogen will be unfavorable entropically.

CHAPTER VI

Addition of Bromonium Nitrate to Unsaturated Systems.

So far we have seen the reactions of iodonium nitrate with unsaturated substrates of various types and structures and also the effect of neighboring groups in the addition reaction. The stereochemical and regiochemical outcome in these reactions were explained by assuming the formation of an intermediate iodonium ion.

Hassner and co-workers[104] have compared the reactivities of iodine azide and bromine azide and found that the former reacted exclusively by an ionic pathway involving a bridged iodonium ion whereas the latter can react either by an ionic or free radical pathway depending upon the nature of the solvent and the presence of oxygen.

Since the electronegativity of bromine is larger than that of iodine[188], bromonium nitrate may be expected to react by both ionic and free radical pathways. But as in the case of iodonium nitrate in chloroform-pyridine, the bromine in bromonium nitrate is also complexed to two pyridine rings. So it was anticipated that bromonium nitrate will also behave like iodonium nitrate, although the higher electrophilicity of bromonium ion may be reflected in its relative reactivity towards unsaturated substrates.

Bromonium nitrate was generated in situ by the reaction of bromine with silver nitrate in chloroform-pyridine. The silver bromide is removed by filtration and the clear light yellow solution

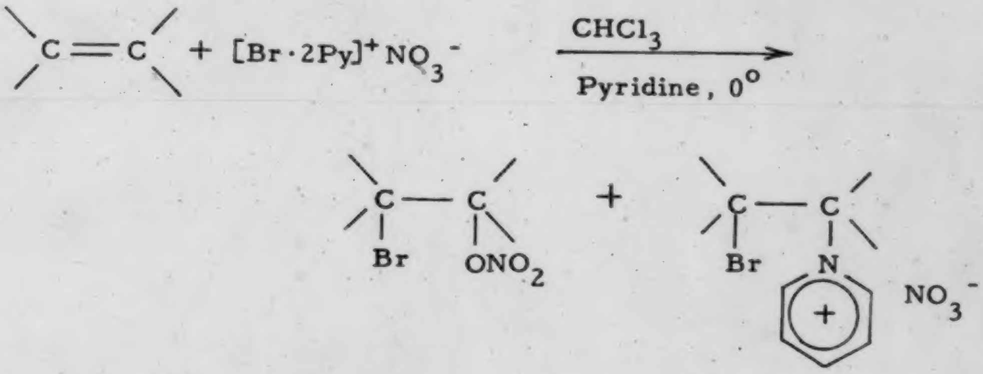
$$AgNO_3 + Br_2 \xrightarrow[\text{Pyridine}]{CHCl_3} [Br\cdot 2Py]^+ NO_3^- + AgBr\downarrow$$

can be used for additions to unsaturated substrates.

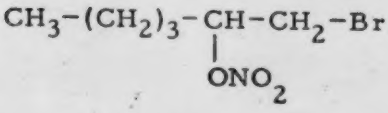
Reactions with Acyclic Terminal Alkenes.

Reaction of bromonium nitrate in chloroform-pyridine with simple alkenes gave products of the type shown in equation 4.

[4]

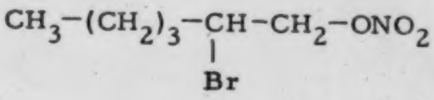

+ [Br·2Py]⁺NO₃⁻
CHCl₃
Pyridine, 0°
Br
ONO₂
+
Br
N
+
NO₃⁻

In contrast to the addition of iodonium nitrate to hex-1-ene, which gave only Markovnikov-type addition products, bromonium nitrate gave 1-bromohex-2-yl nitrate, 213 and 2-bromohex-1-yl nitrate, 214 in a combined yield of 49% and in a ratio of 67:33. The bromopyridinium salt produced in this reaction in 34% yield was a mixture of two isomers, 215 and 216 in a ratio of *ca*. 60:40. Assignments of



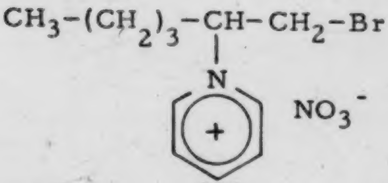
$CH_3-(CH_2)_3-\underset{ONO_2}{\underset{|}{CH}}-CH_2-Br$

213

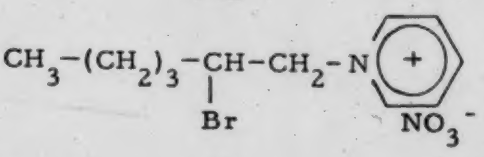


$CH_3-(CH_2)_3-\underset{Br}{\underset{|}{CH}}-CH_2-ONO_2$

214


CH₃-(CH₂)₃-CH-CH₂-Br
N
+
NO₃⁻

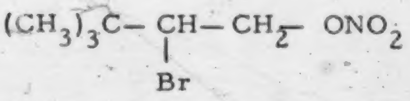
215


CH₃-(CH₂)₃-CH-CH₂-N
Br
+
NO₃⁻

216

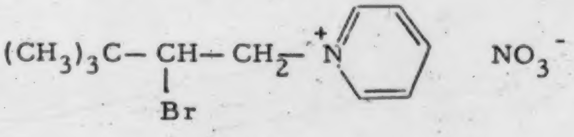
structures to these and similar products and determination of product ratios were done by n.m.r. spectroscopy. It was observed that methine protons alpha to an ONO_2 group absorb in the range 4.8-5.4 δ, whereas protons alpha to a bromo function absorb in the range 3.8-4.5 δ. The methylene protons alpha to a bromo function absorb at about 3.5 δ, whereas methylene protons alpha to a nitrate function absorb at 4.5-5 δ. The presence of a pyridine group in structures such as 215 deshields the methylene protons alpha to the bromine by about 0.7-0.9 p.p.m.

As in iodonium nitrate additions, steric factors appear to play an important role directing the approach of the nitrate ion and pyridine to the initially formed bromonium ion. Thus in the case of 3,3-dimethylbut-1-ene the bromonitrate ester 217 and the bromopyridinium nitrate 218 with the nitrate group and pyridine respectively at the primary position are the products obtained as clearly demonstrated by the n.m.r. spectra.



$(CH_3)_3C-\underset{\displaystyle Br}{CH}-CH_2-ONO_2$

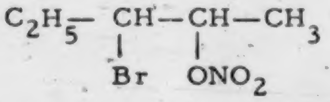
217



218

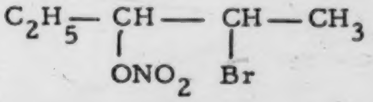
Reactions with Acyclic Non-terminal Alkenes.

Reaction of bromonium nitrate in chloroform-pyridine with Z-pent-2-ene gave a mixture of 3-bromopent-2-yl and 2-bromopent-3-yl nitrates, 219 and 220, in a ratio of 64:36, together with the isomeric bromopyridinium nitrates, 221 and 222, in a ratio of 70:30. For



$C_2H_5-\underset{\displaystyle Br}{CH}-\underset{\displaystyle ONO_2}{CH}-CH_3$

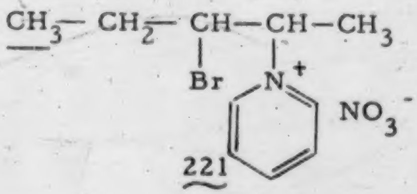
219

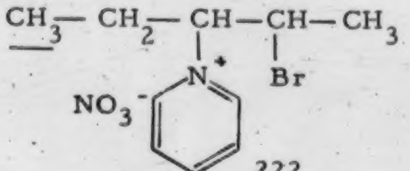


$C_2H_5-\underset{\displaystyle ONO_2}{CH}-\underset{\displaystyle Br}{CH}-CH_3$

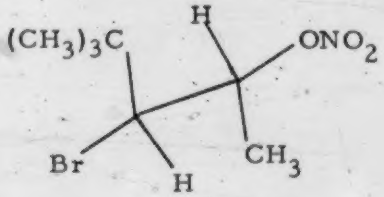
220

the pyridinium salts, the isomer ratio was determined by comparing the n.m.r. intensities of the methyl (underlined in structures 221 and 222) signals which appeared as triplets at δ 1.1 and 0.75 respectively.


221

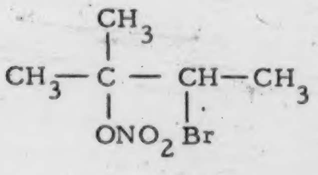

222

In the case of E-4,4-dimethylpent-2-ene, the greater bulk of the *tert.*-butyl group ensures regiospecific addition of bromonium nitrate, the sole product being the bromonitrate ester 223, which was

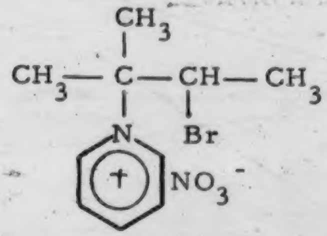

223

formed in 80% yield. No isolable yield of the corresponding bromopyridinium salt was formed in this reaction.

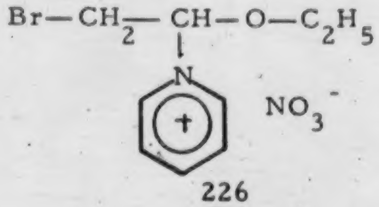
2-Methylbut-2-ene with bromonium nitrate afforded the bromonitrate ester 224 as the major product together with a small yield of the corresponding bromopyridinium nitrate 225. On the other


$CH_3-\underset{ONO_2}{\overset{CH_3}{C}}-\underset{Br}{CH}-CH_3$

224


225

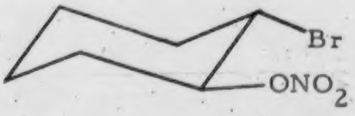
hand ethyl vinyl ether, an example in which the carbonium ion involved is considerably stabilized gave only the bromopyridinium nitrate 226.



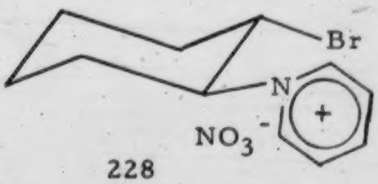
226

Reactions with Cyclic Monounsaturated Compounds.

As in the case of iodonium nitrate additions, addition of bromonium nitrate to cyclic olefins allows a preliminary examination of the stereochemistry of the reaction. Cyclohexene gave the bromonitrate ester 227 in 52% yield which has a *trans*-diequatorial conformation as shown by the n.m.r. spectrum. This demonstrates a *trans* stereospecific addition. The corresponding bromopyridinium nitrate 228 was formed in 31.5% yield.

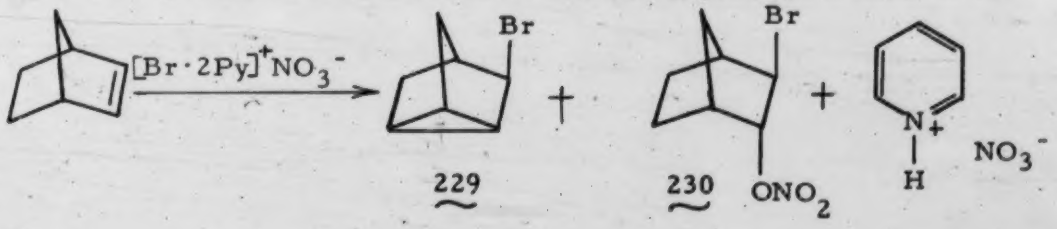


227



228

Norbornene gave nortricyclanyl bromide 229 in 50% yield and the expected bromonitrate ester 230 in 15% yield. They were readily separated by fractional distillation. No bromopyridinium nitrate was produced in this reaction, but a stoichiometric amount of

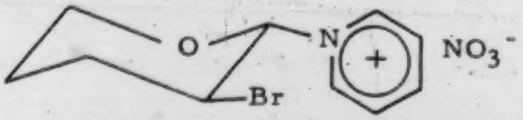


229

230

pyridinium nitrate was formed.

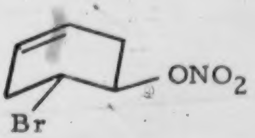
Reaction of 2,3-dihydropyran with bromonium nitrate in chloroform-pyridine afforded in 45% yield trans-equatorial N-(3-bromotetrahydropyranosyl)pyridinium nitrate 231, the n.m.r. spectrum of which compared well with that of the product obtained in the addition of iodonium nitrate to 2,3-dihydropyran. As in the case of ethyl vinyl ether no bromonitrate ester could be isolated in this reaction.



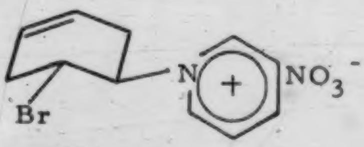
231

Reactions with Unconjugated Dienes.

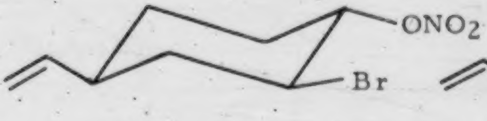
Unconjugated dienes, on reaction with one equivalent of bromonium nitrate, gave only mono-addition products. Thus 1,4-cyclohexadiene gave 5-bromocyclohexen-4-yl nitrate 232 in 54% yield and N-[4-(5-bromocyclohexenyl)] pyridinium nitrate 233 in 25% yield. The fact that a cyclic alkene is more reactive than an acyclic alkene in the same model towards bromonium nitrate is exemplified by its reaction with 4-vinylcyclohexene which gave the bromonitrate ester 234 in 35% yield and the bromopyridinium nitrate 235 in 40% yield corresponding exclusively to addition in the ring. The positions of bromine and nitrate groups in 234 and the bromine and pyridinium



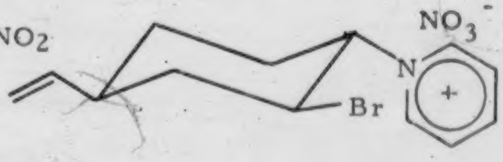
232



233



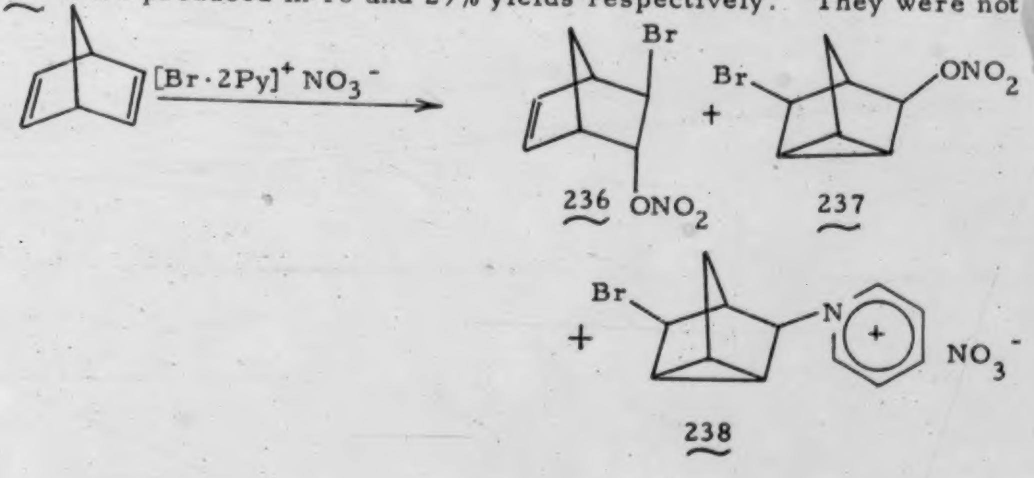
234



235

groups in 235 on the 1,2-cyclohexane bond could not be assigned unambiguously. As in iodonium nitrate additions the marked preference for electrophilic additions in this case to the cyclic olefinic bond may be ascribed to the greater stability of the resulting bromonium ion.

The addition of bromonium nitrate to norbornadiene shows the reduced propensity for neighboring π -bond participation than in iodonium nitrate additions. In the latter case, only products corresponding to cross-ring interaction were formed. On the other hand reaction of bromoniun nitrate with norbornadiene produced two bromonitrate esters and one bromopyridinium nitrate. 3-Bromo-5-norbornen-2-yl nitrate, 236 and tricyclo$\left[2\cdot2\cdot1\cdot0^{2.6}\right]$-5-bromohept-3-yl nitrate, 237 were produced in 16 and 29% yields respectively. They were not

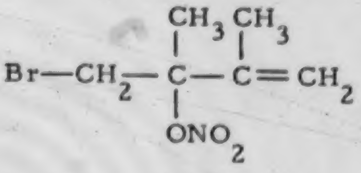


separable by distillation. The structure of 236 was evident from the n.m.r spectrum of the mixture, which showed olefinic hydrogen signals at $\delta_{\text{TMS (CDCl}_3)}$: 6.3. The bromopyridinium salt formed in 12% yield in this reaction was exclusively N-[3-(5-bromonortricyclanyl)] pyridinium nitrate 238; corresponding to cross-ring interaction. The n.m.r. spectrum of 238 compared well with that of the corresponding iodopyridinium nitrate.

Reactions with Conjugated Dienes.

In contrast to the addition of iodonium nitrate to conjugated dienes, which gave only the iodopyridinium salts corresponding to 1,2-addition, the reaction of bromonium nitrate gave significant yields of bromonitrate esters.

Reaction of bromonium nitrate with 2,3-dimethyl-1,3-butadiene gave three products. The bromonitrate ester formed in 31% yield corresponded to the kinetically controlled 1,2-addition product, 239. This was evident from the n.m.r. spectrum of the product soon after isolation (Figure 6). The olefinic hydrogens absorbed as a



$$Br{-}CH_2{-}\overset{CH_3}{\underset{ONO_2}{C}}{-}\overset{CH_3}{C}{=}CH_2$$

239

multiplet at $\delta_{\text{TMS (CDCl}_3)}$: 5.12, while the -$CH_2$-Br group appeared as an AB quartet at δ 3.55 and 3.85 (J=11 Hz). The methyl group attached to the olefinic carbon absorbed as a multiplet (allylic coupling) at δ 1.82, while the other methyl group appeared as a singlet at δ 1.73.

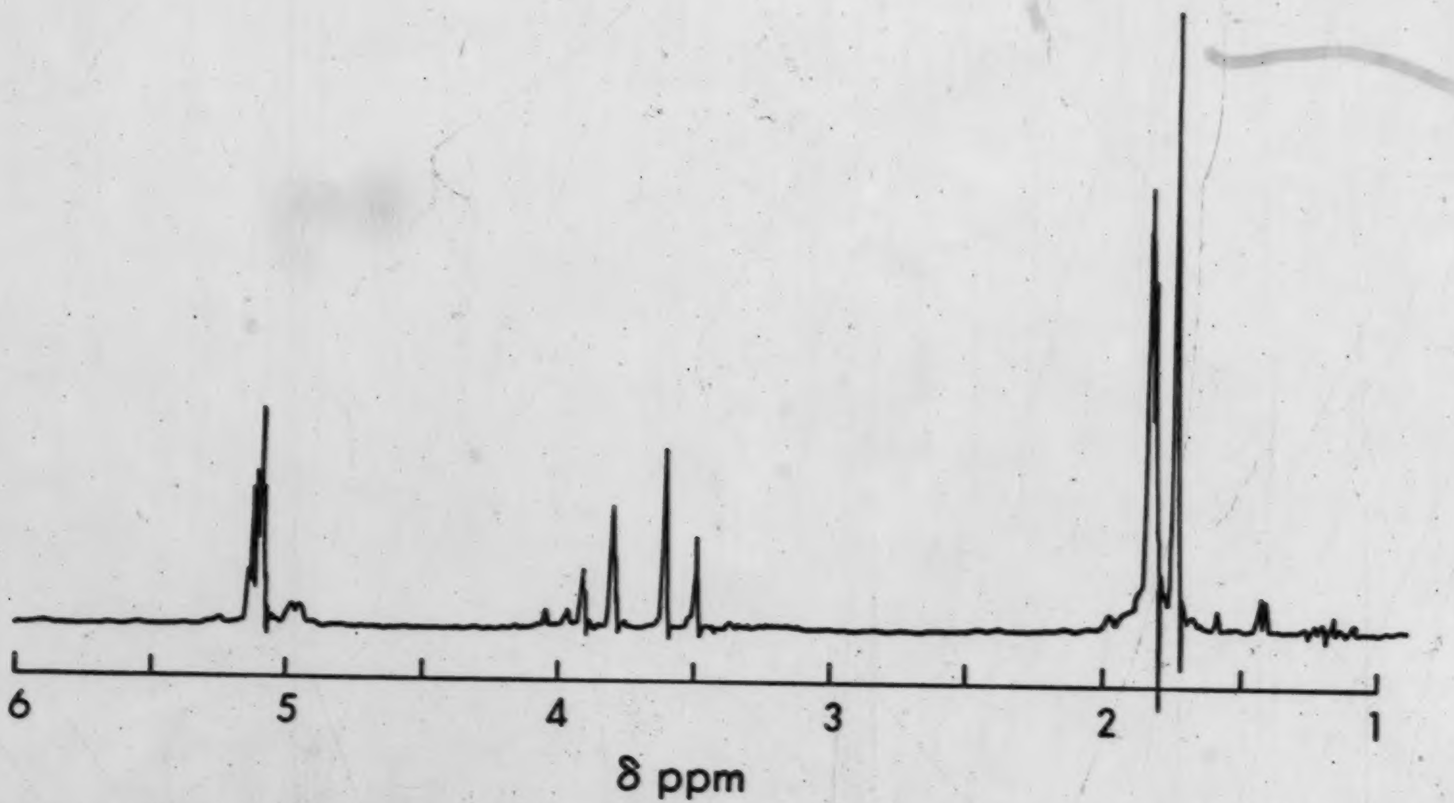
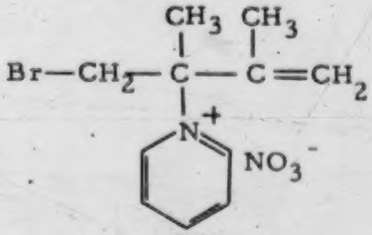
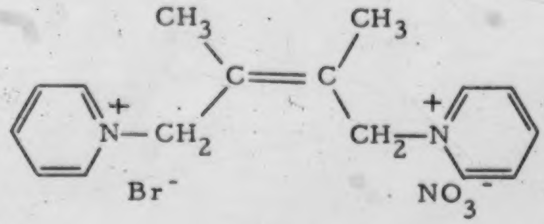


Figure 6. Proton magnetic resonance spectrum at 100 MHz (500 Hz sweep width, 100 Hz offset) in $CDCl_3$ of 2,3-dimethyl-1,3-butadiene-bromonium nitrate adducts, 239, 1 h after isolation. The signals at δ3.97, 4.04, 4.95 and 4.98 correspond to the rearranged product, 245.

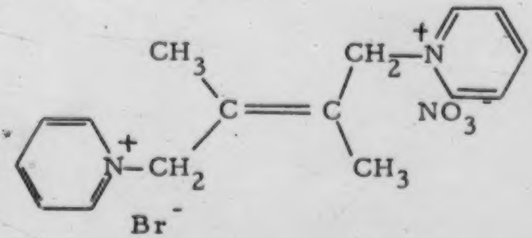
In addition, two pyridinium salts were also formed which were readily separated by crystallization. The major product is assigned structure 240, corresponding to 1,2-addition on the basis of the n.m.r. spectrum, which was comparable with that of 55 formed in iodonium nitrate addition. The n.m.r. spectrum of the other pyridinium salt was identical to that of 56. Although the spectrum is consistent with either the *cis*, 241a or the *trans* structure, 241b, the product was shown to be an approximately equimolar mixture of both



240



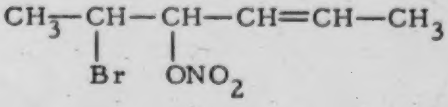
241a



241b

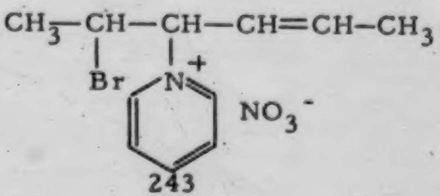
241a and 241 b (*vide infra*).

2,4-Hexadiene behaved similarly. The bromonitrate ester, 242 was produced in 19% yield. In this case the two pyridinium salts 243 and 244 were not separable by crystallization.

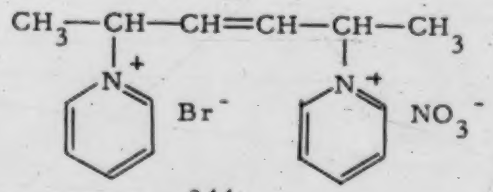


$$CH_3-\underset{Br}{CH}-\underset{ONO_2}{CH}-CH{=}CH-CH_3$$

242

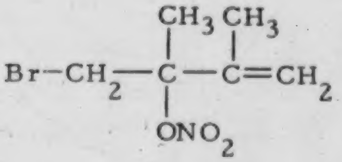


243



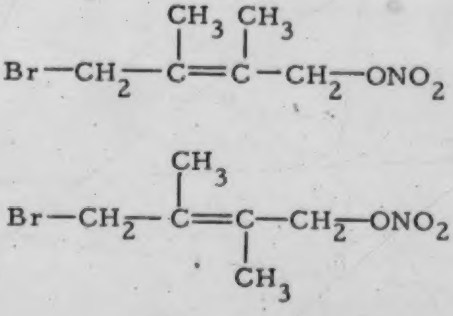
244

An interesting characteristic of these allyl nitrates is their tendency to rearrange tothe thermodynamically more stable 1,4-bromonitrates. Thus both 239 and 242 rearrange either in the liquid phase or in solution to 245 and 246 respectively. The rearrangement can be followed by n.m.r. spectroscopy. Figures 6-8 show the n.m.r. spectra of the bromonitrate ester from 2,3-dimethyl-1,3-butadiene at different times after its isolation. In the case of 239 the rearranged



$\mathrm{Br{-}CH_2{-}C(CH_3)(ONO_2){-}C(CH_3){=}CH_2}$

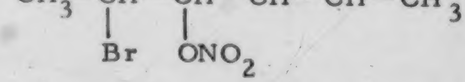
239



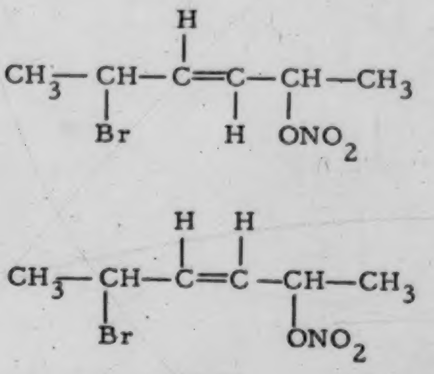
$\mathrm{Br{-}CH_2{-}C(CH_3){=}C(CH_3){-}CH_2{-}ONO_2}$

$\mathrm{Br{-}CH_2{-}C(CH_3){=}C(CH_3){-}CH_2{-}ONO_2}$

245a, b



$\mathrm{CH_3{-}CH(Br){-}CH(ONO_2){-}CH{=}CH{-}CH_3}$



$\mathrm{CH_3{-}CH(Br){-}CH{=}CH{-}CH(ONO_2){-}CH_3}$

$\mathrm{CH_3{-}CH(Br){-}CH{=}CH{-}CH(ONO_2){-}CH_3}$

246a, b

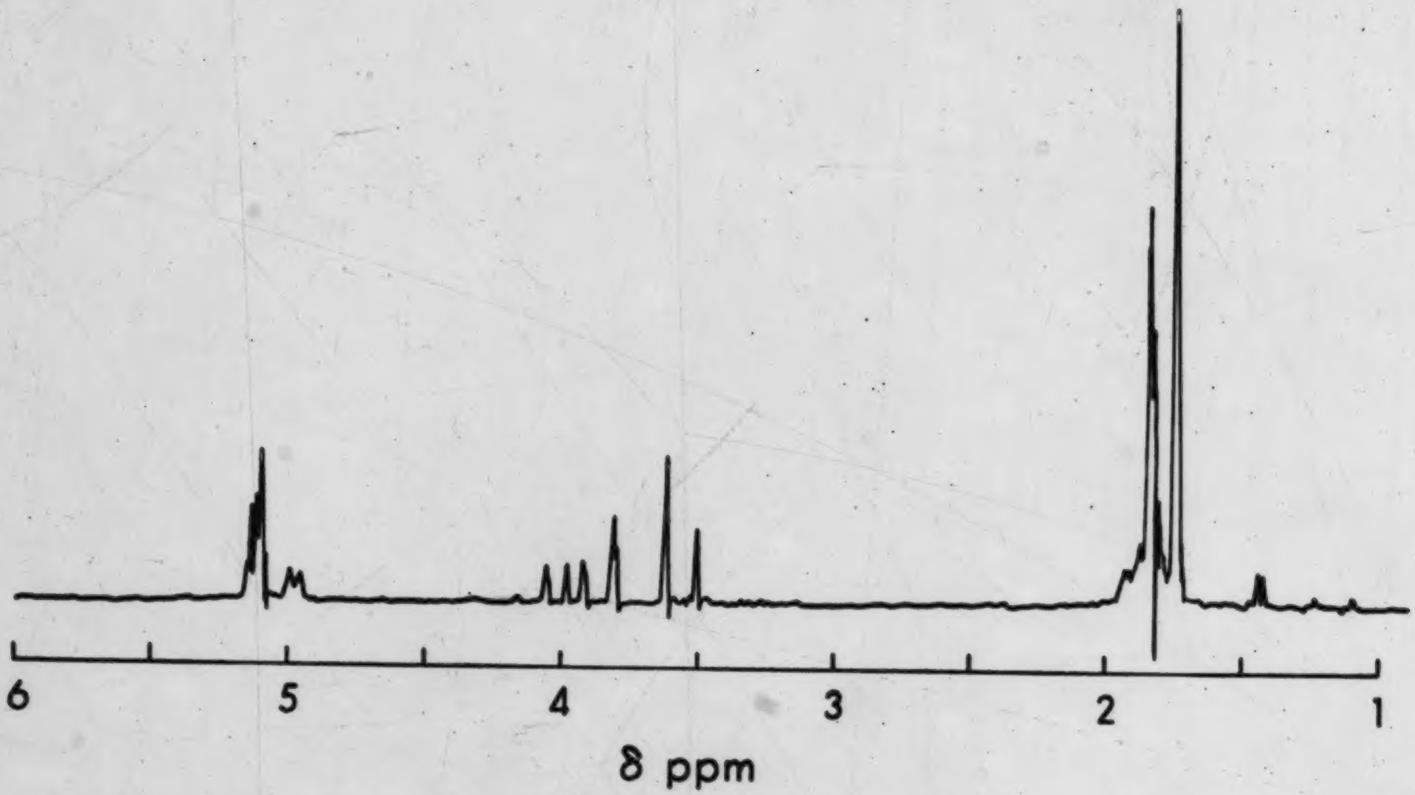


Figure 7. Proton magnetic resonance spectrum at 100 MHz (500 Hz sweep width, 100 Hz offset) in $CDCl_3$ of 2,3-dimethyl-1,3-butadiene-bromonium nitrate adduct 3 h after isolation.

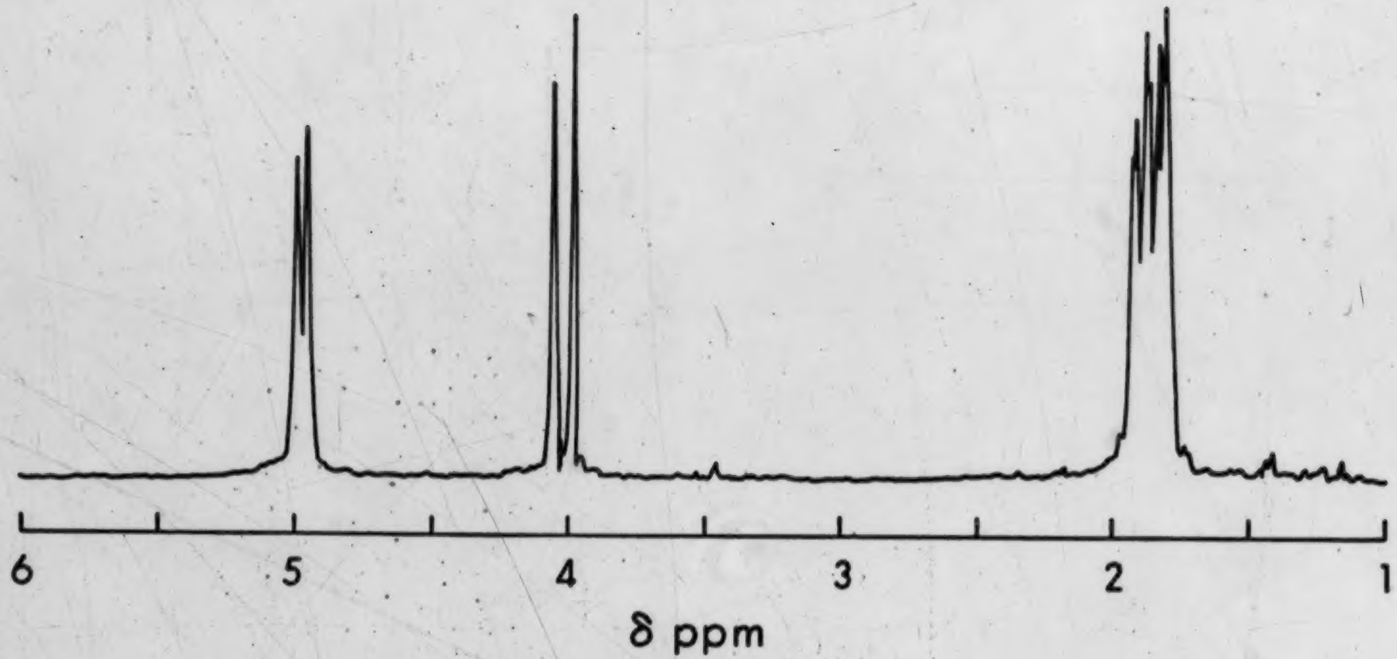


Figure 8. Proton magnetic resonance spectrum at 100 MHz (500 Hz sweep width, 100 Hz offset) in $CDCl_3$ of 2,3-dimethyl-1,3-butadiene-bromonium nitrate adduct after complete rearrangement to 245.

product was a mixture of two isomers in approximately equal amounts as shown by high pressure liquid chromatography. Figure 8 shows the n.m.r. spectrum of the rearranged product. The $-CH_2Br$ groups appear as two singlets at $\delta_{TMS}(CDCl_3)$: 3.97 and 4.04, while the $-CH_2-ONO_2$ groups absorb as two singlets at δ 4.95 and 4.98. On this basis structures 245a and 245b are assigned to the products. Moreover, treatment of the mixture with pyridine in chloroform at room temperature gave 241 in almost quantitiative yield. This proves that product 241 is a mixture of two geometrical isomers 241a and 241b.

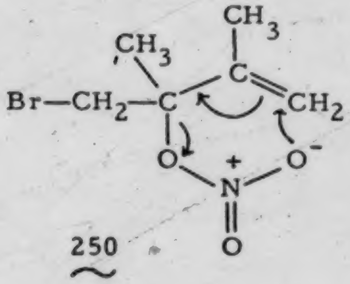
The rearranged product from 242 was predominantly the *trans*-isomer 246a as shown by the n.m.r. spectrum, although high pressure liquid chromatography showed the presence of a minor product, probably the *cis*-isomer 246b. The n.m.r. spectrum of 246 showed δ_{TMS} $(CDCl_3)$: 1.43 (d, 3H, $\underline{CH_3}-CH-ONO_2$, J=6.5 Hz); 1.78 (d, 3H, $\underline{CH_3}-CH-Br$, J=7 Hz); 4.65 (quint, 1H, $-CH-Br$, J=7 Hz); 5.5 (m, 1H, $-CH-ONO_2$). The olefinic hydrogens appeared as an octet centered at δ 5.92 with $J_{CH=CH}$ = 14.5 Hz, from which follows the *trans*-stereochemistry about the olefinic bond.

Treatment of 246 with pyridine in chloroform gave 244 in quantitative yield. The n.m.r. spectrum of 244 showed two identical methyl groups which absorbed as a doublet at $\delta_{TMS}[(CD_3)_2SO]$: 1.80. The other signals were at δ 5.8 (m, 2H, 2 $-CH-\overset{+}{N}\lesseqgtr$); 6.15-6.5 (m, 2H, olefinic hydrogens); 8.1-9.3 (m, 10H, pyridine hydrogens).

Compounds 241 and 244, corresponding to 1,4-addition may be envisaged as arising by two pathways (Scheme 12). a) The initially formed bromonium ion intermediate 247 can open up to the resonance stabilized allylic cation, 248 which can undergo nucleophilic attack at the terminal carbon atom to give the thermodynamically more stable 1,4-addition product 249. The allylic bromine can then be displaced by pyridine to give 241. Alternatively, b) the initially formed allyl nitrate 239 can rearrange to the thermodynamically more stable 1,4-bromonitrate, 245. Nucleophilic displacement of allylic bromine and nitrate in 245 by pyridine can lead to 241.

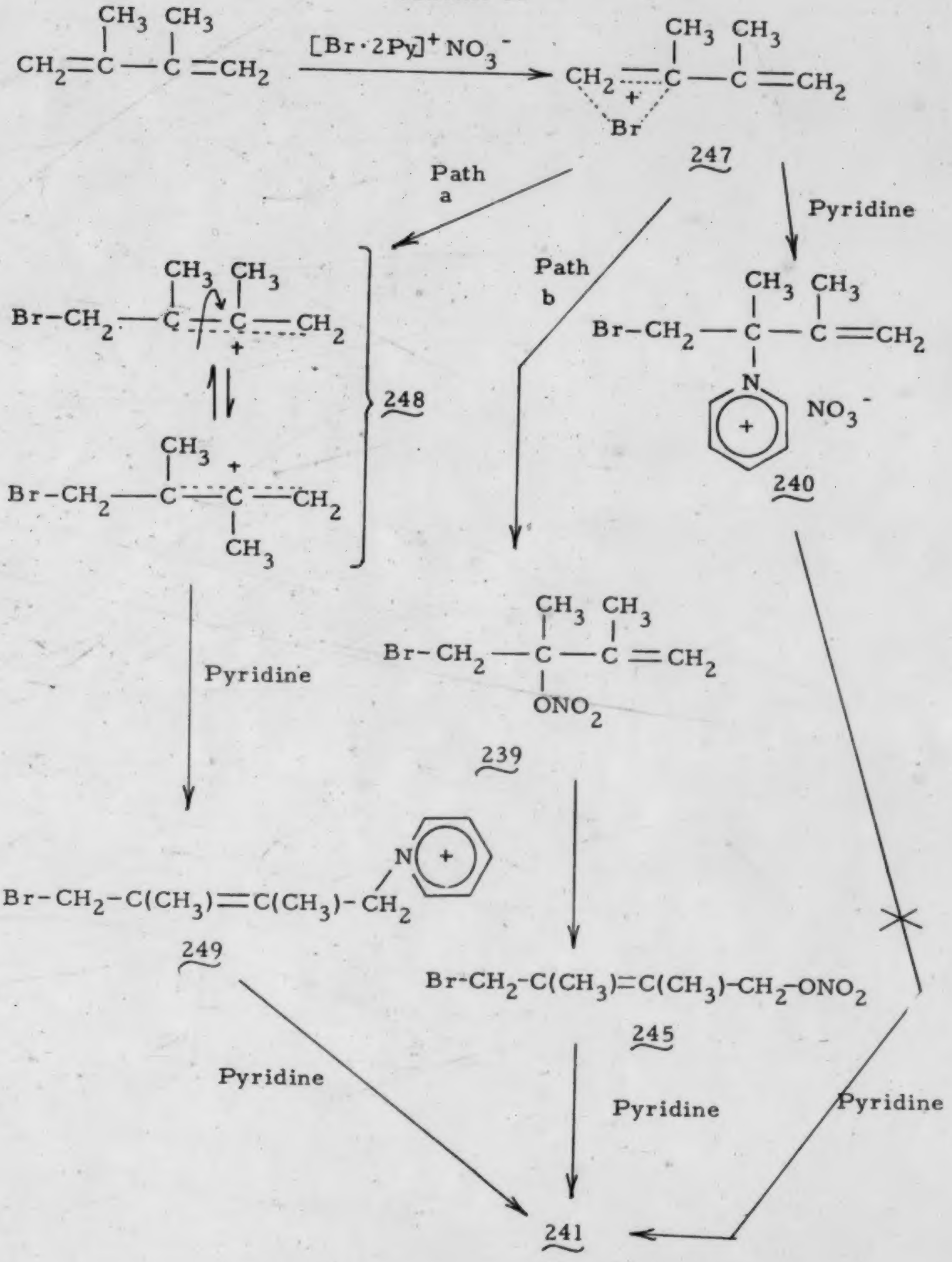
To distinguish between these two possibilities, the reaction between bromonium nitrate and 2,3-dimethyl-1,3-butadiene was allowed to proceed for a longer time. The yield of 1,4-addition product was found to increase (ca. 8% after $3\frac{1}{2}$ h, 16.5% after 12 h). Since the rearrangement of 239 to 245 is slow and since no equilibration of benzylic center is observed in the addition of bromonium nitrate to *Z*-*β*-deuterostyrene (*vide infra*), it is reasonable to assume that products of the type 241 are formed by path b. A similar mechanism may be operating in the addition of iodonium nitrate to 2,3-dimethyl-1,3-butadiene.

As far as the mechanism of rearrangement of 239 to 245 and of 242 to 246 is concerned, one can visualize two possible pathways. First the bromonitrate ester 239 can ionize to the allylic cation 248 and nitrate ion which can recombine to give the more stable 1,4-addition product. Alternatively, it can proceed by a concerted mechanism involving a six-membered cyclic transition state 250. Such a



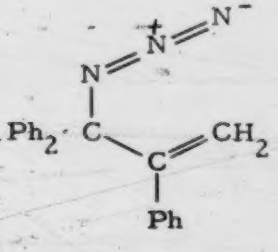
250

Scheme 12

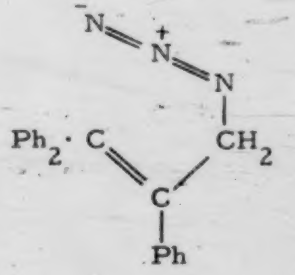


$[Br\cdot 2Py]^+ NO_3^-$
247
Path a
Path b
Pyridine
248
240
NO_3^-
Pyridine
239
Br-CH₂-C(CH₃)=C(CH₃)-CH₂
249
Br-CH₂-C(CH₃)=C(CH₃)-CH₂-ONO₂
245
Pyridine
Pyridine
Pyridine
241

concerted mechanism has been postulated by Hassner for the rearrangement of the allyl azide 251 to 252[106]. Although we do not have enough



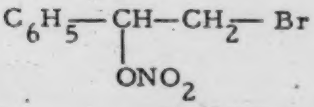
251



252

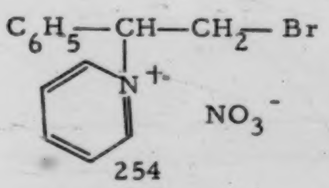
evidence to prove or disprove either mechanism, we feel that the concerted mechanism may be operating, since the rearrangement can proceed either in the liquid phase or in a weakly ionizing solvent like chloroform.

Reaction of styrene with bromonium nitrate gave the bromonitrate ester 253 as the major product (49%). The pyridinium salt produced in this reaction was a mixture of 254 and 255 as shown by the n.m.r. spectrum. The mixture was converted into 255 in an

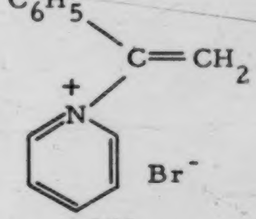


$C_6H_5-\underset{\displaystyle ONO_2}{CH}-CH_2-Br$

253



254



255

overall yield of 26.5% by treatment with potassium carbonate.

Reactions with Acetylenic Compounds.

Like iodonium nitrate, bromonium nitrate was unreactive towards non-terminal acetylenes. With terminal acetylenes alkynyl bromides were formed together with a stoichiometric quantity of pyridinium nitrate. Thus phenylacetylene gave a 63% yield of

$$\mathrm{Ph{-}C{\equiv}C{-}Br}$$

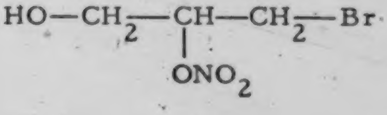
256

β-bromophenylacetylene, 256.

Reactions with Olefinic Alcohols.

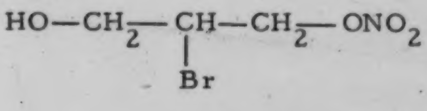
In Chapter III, we have seen the reactions of iodonium nitrate both in chloroform-pyridine and chloroform-sym-collidine with various olefinic alcohols which gave normal addition products and/or cyclic ethers depending upon the structure of the olefinic alcohols. The reactivity of bromonium nitrate in chloroform-pyridine towards a few olefinic alcohols was examined.

Allyl alcohol on reaction with bromonium nitrate gave two isomeric bromonitrate esters. 3-Hydroxy-1-bromoprop-2-yl nitrate, 257 and 3-hydroxy-2-bromoprop-1-yl nitrate, 258 were formed in a combined yield of 31% and in a ratio of 69:31, as determined by n.m.r. The accompanying bromopyridinium salt was also a mixture of two



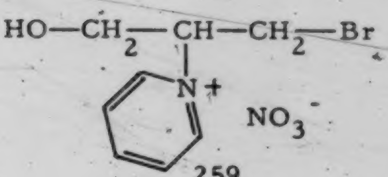
$$\mathrm{HO{-}CH_2{-}CH(ONO_2){-}CH_2{-}Br}$$

257

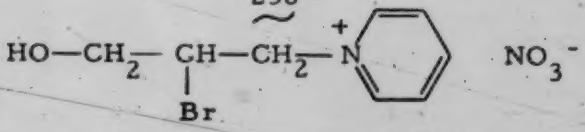


$$\mathrm{HO{-}CH_2{-}CH(Br){-}CH_2{-}ONO_2}$$

258



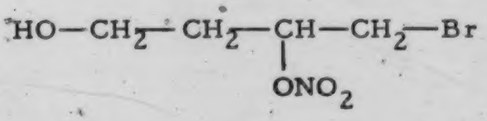
259



260

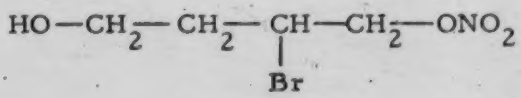
regioisomers, 259 and 260. The isomer ratio could not be determined in this case by n.m.r. because of overlapping signals.

But-3-en-1-ol also gave a comparable result. The bromonitrate esters, 261 and 262 were formed in 33% yield (isomer ratio 67:33). The pyridinium salt consisted of two isomers, 263 and 264 in a ratio of 85:15.



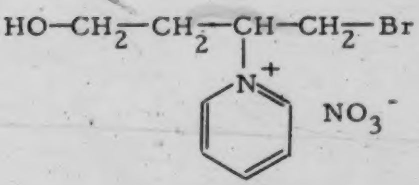
$\mathrm{HO{-}CH_2{-}CH_2{-}\underset{\displaystyle ONO_2}{\underset{|}{CH}}{-}CH_2{-}Br}$

261

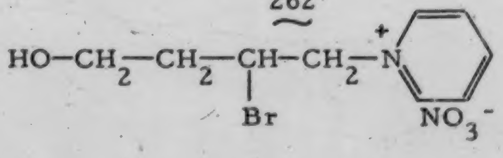


$\mathrm{HO{-}CH_2{-}CH_2{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH_2{-}ONO_2}$

262

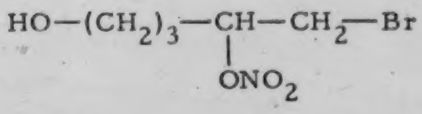


263



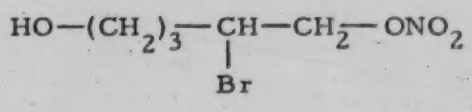
264

The reaction of bromonium nitrate with pent-4-en-1-ol gives an opportunity to compare the extent of neighboring hydroxy group participation in this and iodonium nitrate additions. The major product in this case was a mixture of bromonitrate esters, 265 and 266 formed in 29% yield and in a ratio of 67:33. The cyclic ether, 2-bromomethyl-tetrahydrofuran, 267 was produced in only 20% yield as compared to 60% in iodonium nitrate addition. In addition the



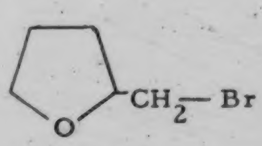
$\mathrm{HO{-}(CH_2)_3{-}\underset{\displaystyle ONO_2}{\underset{|}{CH}}{-}CH_2{-}Br}$

265

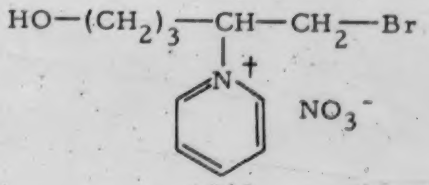


$\mathrm{HO{-}(CH_2)_3{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH_2{-}ONO_2}$

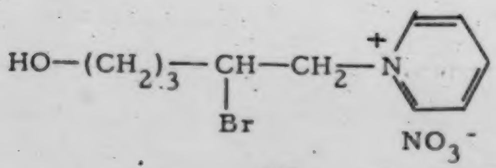
266



267



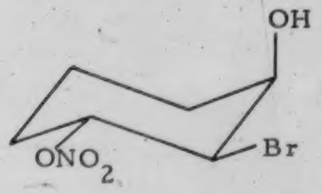
268



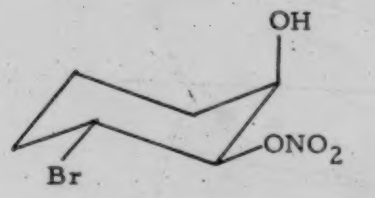
269

isomeric bromopyridnium nitrates, 268 and 269 were formed in approximately 20% yield (ratio 60:40).

Cyclohex-2-en-1-ol, on reaction with bromonium nitrate gave a mixture of at least three bromonitrate esters in 52% yield and more than one bromopyridinium nitrate in 23.5% yield. Of the bromonitrates the major isomer was 270, which is derived from a bromonium ion formed *cis* to the hydroxy group. Another isomer is assigned structure 271 which is derived from a bromonium ion formed *trans* to



270

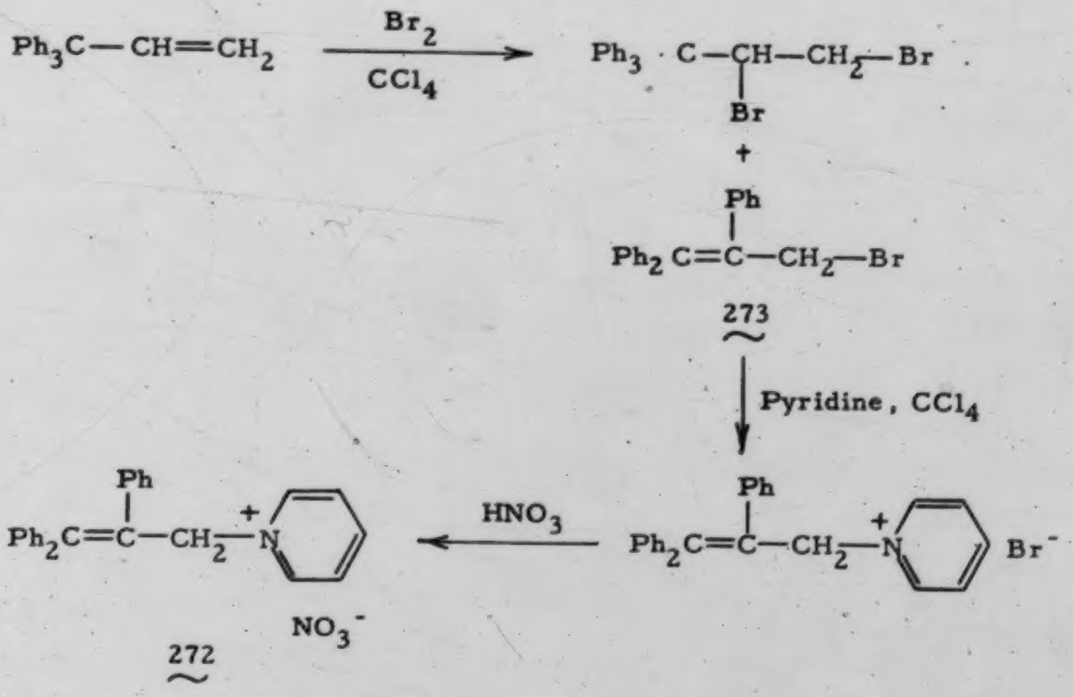


271

the hydroxy group. Compound 271 had the -CH-ONO_2 absorption in the n.m.r. spectrum at δ 5.14 as a quartet superimposed on a multiplet. The structure of the third isomer could not be assigned.

As in the case of iodonium nitrate addition, the structures of the bromopyridinium salts could not be assigned unambiguously.

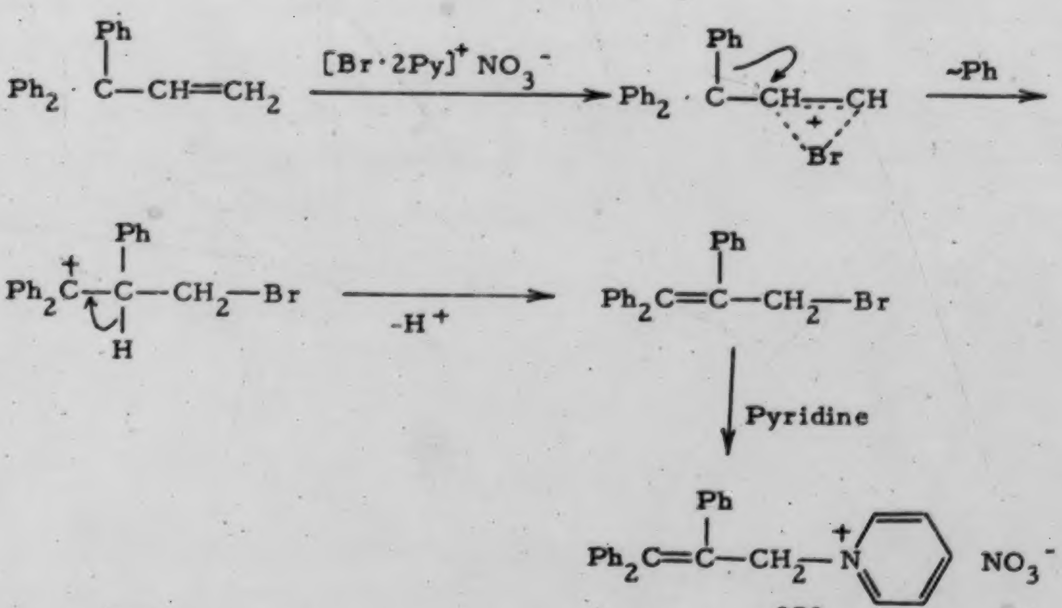
3,3,3-Triphenylpropene was unreactive towards iodonium nitrate. On the other hand it did react with bromonium nitrate. The product formed in 73% yield is assigned structure 272 on the basis of the n.m.r. spectrum, elemental analysis and synthesis from the allyl bromide, 273. The allylic bromide, 273 is one of the products formed in the addition of bromine to 3,3,3-triphenylpropene[149].


Ph3C—CH═CH2
Br2
CCl4
Ph3 · C—CH—CH2—Br
Br
+
Ph
Ph2 C═C—CH2—Br
273
Pyridine, CCl4
HNO3
Ph
Ph2C═C—CH2—N+
Br-
Ph
Ph2C═C—CH2—N+
NO3-
272

In the n.m.r. spectrum of 272, one of the phenyl groups was different from the other two and absorbed at about 0.4 p.p.m. downfield. The integration showed the presence of one pyridine per molecule. In addition there was a singlet at δ 5.72 integrating for two hydrogens. This is assigned to the methylene hydrogens.

Compound 272 may be envisaged as arising as a result of phenyl migration as shown in Scheme 13.

Scheme 13

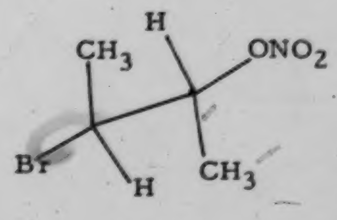


272

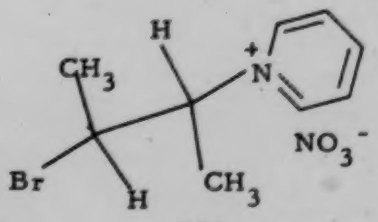
Stereochemistry and Mechanism.

The addition of bromonium nitrate to cyclohexene is stereospecifically *trans*. In acyclic systems this was established by performing additions to three (*Z*) and (*E*)-pairs of olefins and confirmed by addition to (*Z*)-β-deuterostyrene.

(*E*)-But-2-ene on reaction with bromonium nitrate in chloroform-pyridine afforded the bromonitrate ester 274 and the bromopyridinium nitrate 275 in 44 and 37% yields respectively. Parallel

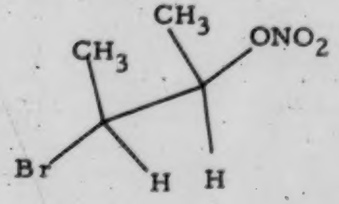


274

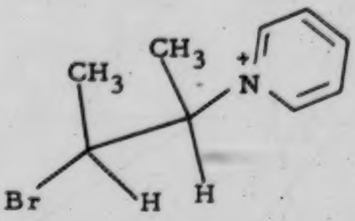


275

addition to (Z)-but-2-ene produced the bromonitrate ester 276 in 48% yield and the bromopyridinium nitrate 277 in 29% yield. The bromo-


CH3
CH3
ONO2
Br
H
H

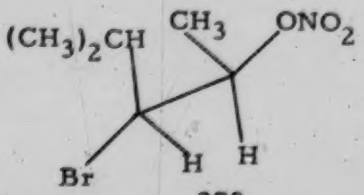
276


CH3
CH3
+N
Br
H
H

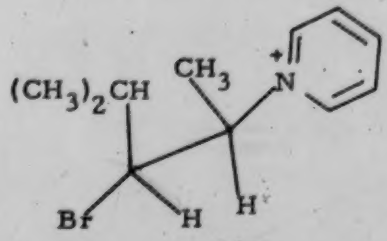
277

nitrate esters were evidently different as shown by the n.m.r. spectra, so were the bromopyridinium nitrates.

The addition of bromonium nitrate to (Z) and (E)-4-methylpent-2-enes also gave stereoisomeric products as clearly shown by the n.m.r. spectra. In the case of the (Z)-isomer the reaction was regiospecific and stereospecific in the formation of the bromonitrate ester 278 and the bromopyridinium nitrate 279, whereas for the (E)-isomer, the reaction was stereospecific and regioselective. The bromonitrate esters 280 and 281 were produced in a ratio of 74:26. The ratio of

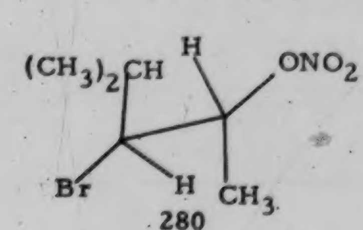

(CH3)2CH
CH3
ONO2
Br
H
H

278

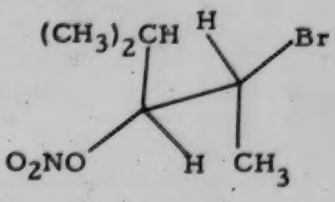

(CH3)2CH
CH3
+N
Br
H
H

279

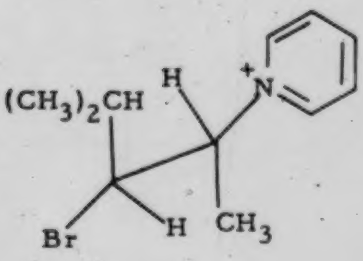
the corresponding bromopyridinium salts 282 and 283 was also approximately the same as for the bromonitrate esters.


(CH3)2CH
H
ONO2
Br
H
CH3

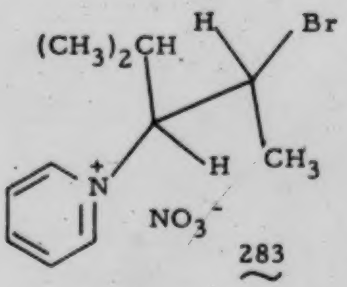
280


(CH3)2CH
H
Br
O2NO
H
CH3

281

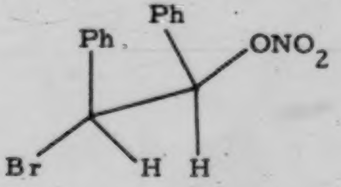


282

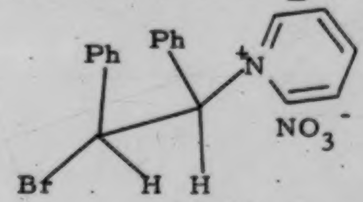


283

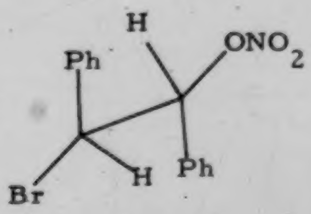
The reaction of bromonium nitrate with (Z) and (E)-stilbenes was also stereospecific in the formation of the bromonitrate esters 284 and 286 and the bromopyridinium salts 285 and 287. 284 and 285 were produced in 52% and 32% yields respectively from the (Z)-isomer and 286 and 287 in 21 and 63.5% yields respectively from the (E)-isomer.



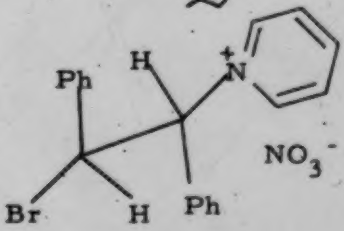
284



285

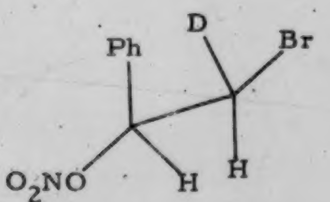


286

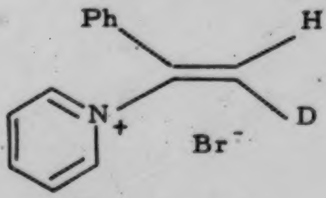


287

To eliminate the possibility that the observed stereospecificity is due to restricted rotation in the intermediate bromocarbonium ions in the additions to (Z) and (E)-stilbenes and to establish conclusively the trans stereospecificity of addition, the reaction of bromonium nitrate with (Z)-β-deuterostyrene (>95% D) was performed. The bromonitrate ester 288 and the alkenyl pyridinium bromide 289 were isolated in 46% and 26.5% yields respectively. In the n.m.r. spectrum of 288 the methine hydrogen absorbed as a doublet at δ_{TMS} ($CDCl_3$): 6.0 (J=7.5 Hz) whereas for the protium analog 253, it absorbed as a quartet at δ_{TMS} ($CDCl_3$): 6.0 (J=6 Hz, 7.5 Hz). The methylene hydrogens in 288 appeared as a doublet further split by H-D coupling at δ_{TMS} ($CDCl_3$): 3.62 (J=7.5 Hz) whereas for 253 the methylene hydrogens absorbed as a triplet at δ_{TMS} ($CDCl_3$): 3.62 (J=6 Hz and 7.5 Hz).



288

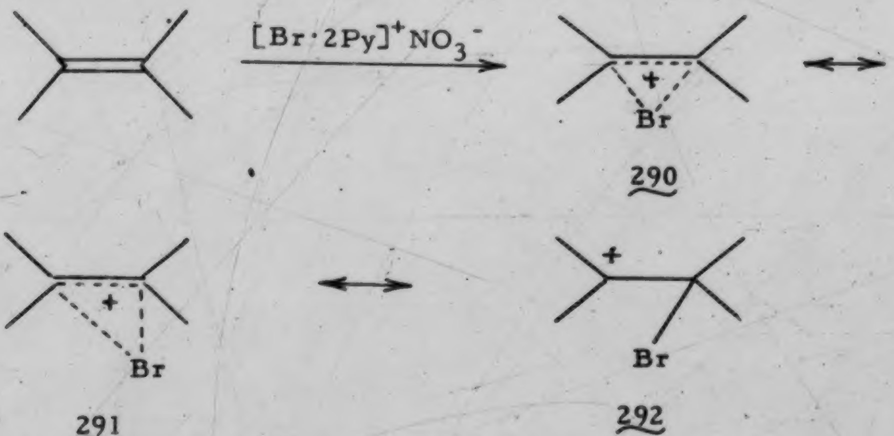


289

The n.m.r. spectrum of 289 was identical to that of 208 formed in iodonium nitrate addition to (*Z*)-β-deuterostyrene.

This conclusively proves that the addition of bromonium nitrate to olefins is stereospecifically *trans* and no equilibration of benzylic centers occurs in the additions to aryl substituted olefins.

The stereochemical and regiochemical outcome in the additions of bromonium nitrate to unsaturated substrates can be explained by an ionic mechanism involving the formation of a three-membered ring bromonium ion intemediate 290, which is opened up from the backside by nucleophilic attack by nitrate ion or pyridine. In the case of unsymmetrically substituted olefins, there can be substantial contribution from the unsymmetrically bridged form 291 and the open cationic form 292 to permit nucleophilic attack despite increased steric hindrance and to permit neighboring hydroxyl group attack to form cyclic ethers. The intermediate can be sufficiently stabilized through the bridged form **291** to maintain its stereochemical integrity to lead to the observed stereospecificity in additions to aryl substituted olefins.



290

291

292

The observed stereospecificity in the additions to stilbenes and to (Z)-β-deuterostyrene and the regiospecificity in the addition to (Z)-β-deuterostyrene eliminate the possibility of any contribution from a free radical component under the conditions in which the above reactions were performed. Free radical contribution results in non-stereospecific addition and a reversal of the regiochemistry as is observed in bromine azide and chlorine azide additions[108].

Like the iodonium nitrate-pyridine complex, the bromonium nitrate-pyridine complex can also be isolated as a white solid. Attempts to purify the material by recrystallization were not successful. Atempted drying of the complex over anhydrous calcium sulfate in a desiccator resulted in a violent explosion.

CHAPTER VII

A Comparison of Iodonium Nitrate, Bromonium Nitrate and Other Pseudohalogens.

The reactions of iodonium nitrate and bromonium nitrate with olefins to give halonitrate esters and halopyridinium salts and with olefinic alcohols to give the corresponding addition products and/or cyclic ethers are quite general. The isolation of substantial quantities of haloalkyl nitrates in the reactions of these pseudohalogens with olefinic substrates in chloroform-pyridine is surprising in view of the reported relative nucleophilicities of pyridine and nitrate (20:1 for aqueous solutions)[189]. However, since the reported heat of hydration of the nitrate ion is -61 ± 2 kcal $(g.\ ion)^{-1}$, [190a] and therefore comparable with that of the iodide ion[190b] [-68 kcal $(g.ion)^{-1}$], then the nucleophilicity of this ion may be expected to be increased relative to that of the unchanged pyridine upon going to an aprotic solvent. No data are available for a more direct comparison.

In all these reactions the products isolated are formed under kinetic control in that, the primary products do not interconvert to any appreciable extent under the reaction conditions. This conclusion is consistent with the observed trans stereochemistry of addition.

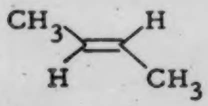
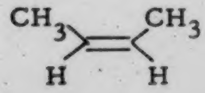
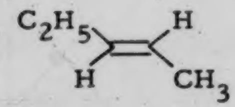
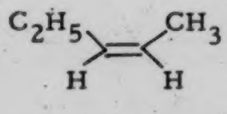
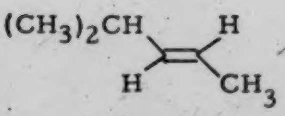
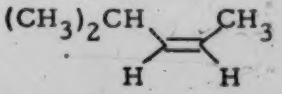
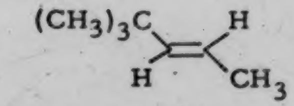
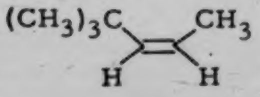
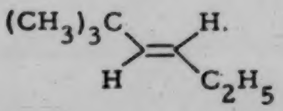
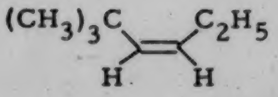
Our study indicates that iodonium nitrate and bromonium nitrate are electrophilic reagents, whose reaction with unsaturated substrates is influenced to a large extent by the steric environment in the olefinic substrate. This is reflected in the regiochemistry of the addition. When the olefinic carbon atom carries especially bulky groups, the incoming nucleophile (pyridine or nitrate ion) is forced to attack the intermediate halonium ion at the sterically more favorable but electronically less favorable carbon (e.g. 3,3-dimethylbut-1-ene).

The relative proportion of regioisomeric iodonitrate esters formed from (Z) and (E)-pairs of olefins (Table 17) shows the effect of alkyl substitution on the regiochemistry of addition. When the methyl group in but-2-ene is successively replaced by $-C_2H_5$, $-CH(CH_3)_2$, and $(CH_3)_3C-$ groups, the isomer in which the nitrate is attached to the carbon carrying the smaller substituent predominates and in the case of a $(CH_3)_3C-$ substituent, this is the only isomer formed.

The ability of solvent pyridine to compete with the nitrate ion for the intermediate halonium ion appears to depend on the steric environment in the olefin and also on the thermodynamic stability of the intermediate halonium ion. Thus, for example, in the additon of iodonium nitrate to 3,3-dimethylbut-1-ene, in which the nucleophilic attack by both nitrate ion and pyridine occurs at the less stable but sterically favorable primary cationic centre, the iodonitrate ester is formed in 26% yield and the iodopyridinium nitrate in 49% yield. On the other hand in the case of (E)-4,4-dimethylpent-2-ene in which the products isolated are derived from nucleophilic attack at the electronically more favorable secondary cationic centre, the proportion of the iodonitrate is considerably increased at the expense of the iodopyridinium nitrate, which is formed only in less than 5% yield. But in the reaction of iodonium nitrate with trisubstituted and tetrasubstituted olefins, the outcome is exactly the reverse. Thus with (Z) and (E)-3-methylpent-2-enes in which the nucleophile enters the sterically unfavorable but thermodynamically more stable tertiary cationic

Table 17

Relative Proportions of Regioisomeric Iodonitrate Esters from (Z) and (E)-pairs of Olefins.

Olefin	Iodonitrate Ester Markovnikov : Anti-Markovnikov
	-
	-
	31 : 69
	30 : 70
	20 : 80
	0 : 100
	0 : 100
	0 : 100
	0 : 100
	0 : 100
$(CH_3)_3CCH{=}CH_2$	0 : 100

centre, the iodopyridinium nitrates are formed to the complete exclusion of other isolable products.

Although iodonium nitrate and bromonium nitrate behave much the same way towards unsaturated substrates, there is some apparent difference in reactivity between the two pseudohalogens. Thus while iodonium nitrate is unreactive towards 3,3,3-triphenylpropene, bromonium nitrate did react with this olefin to give a pyridinium salt. While for iodonium nitrate this inertness may be attributed to steric hindrance in the olefin, the reactivity of bromonium nitrate may reflect its higher electrophilicity which is able to overcome the steric factors. The relative electrophilicities of these two reagents were compared by performing a competition reaction towards E-4,4-dimethylpent-2-ene. The ratio of bromonitrate and iodonitrate esters was determined by n.m.r. spectroscopy which was found to be approximately 4:1. This result suggests that bromonium nitrate is at least 4 times as reactive as iodonium nitrate.

Pent-4-en-1-ol reacts with both iodonium and bromonium nitrates to afford similar types of products. But with bromonium nitrate the proportion of the cyclized product is lower than with iodonium nitrate. This is consistent with the behaviour of pent-4-en-1-ol towards iodine and bromine, where iodine gave a much larger proportion of the cyclic ether[137b].

A major difference between bromonium nitrate and iodonium nitrate is found in their reactions with phenyl, tri- and tetra-substituted olefins. Bromonium nitrate gave substantial yields of the ester whereas iodonium nitrate gave only the pyridinium salts. With other olefinic systems too, the relative yields of pyridinium salts are in general lower in bromonium nitrate additions than in iodonium nitrate additions. If we assume that it is the thermodynamic stability of the intermediate halonium ions which allows solvent pyridine to compete successfully with the nitrate, then the above results give some indication of the relative stability of the three-membered ring iodonium ion versus the three-membered ring bromonium ion. This again is consistent with the relative stabilities of iodonium and bromonium ions involved in halogen azide additions[104].

Bromonium nitrate differs from other positive bromine containing pseudohalogens, for example, bromine azide, in that with this pseudohalogen, even additions to aryl substituted olefins is stereospecifically trans. This result eliminates any contribution from an open bromocarbonium ion. On the other hand addition of bromine azide to such olefinic systems under ionic conditions results in equilibration of benzylic centres suggesting involvement of an open bromocarbonium ion. This difference in behaviour may be attributed to complexation with pyridine in the case of bromonium nitrate.

Iodonium nitrate compares with iodine isocyanate in its reactivity with olefinic substrates[8,12]. Thus like iodine isocyanate, iodonium nitrate is unreactive towards α,β-unsaturated carbonyl compounds. But it differs from iodine isocyanate in that it reacts with stilbenes. Also, whereas no neighboring hydroxy group participation is encountered in iodine isocyanate additions, reaction of iodonium nitrate with suitable olefinic substrates affords cyclic ethers.

The behaviour of iodonium nitrate is to be contrasted with the closely related iodine nitrite or nitryl iodide[21]. Whereas the former reacts as a source of electrophilic iodine, the latter reacts by a free radical mechanism acting as a source of nitryl radical.

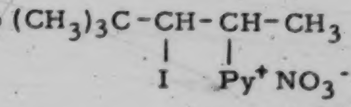
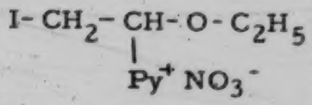
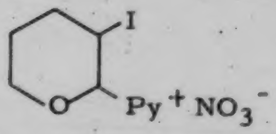
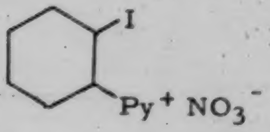
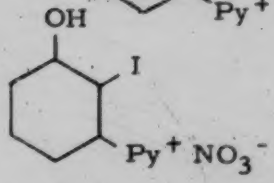
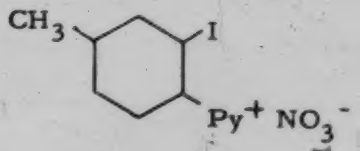
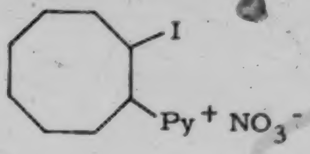
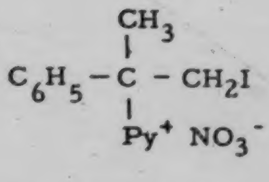
As mentioned in the introduction, we were interested in preparing a series of iodoalkyl pyridinium salts and alkenyl pyridinium salts for biological evaluation. A good number of them, especially the alkenyl pyridinium iodides were found to possess significant oral anti-diabetic property. The results are summarized in Table 18. As is evident from the Table, the saturated pyridinium salts are in general inactive whereas the unsaturated ones are active. Although it is difficult to draw any structure activity correlation, the parent N-[1-(1-phenylethenyl)]pyridinium iodide appears to be the most active. These data can be used to modify structures for optimum activity.

Although it is difficult at this stage to draw any conclusion as to the synthetic potential of these reactions, they provide a satisfactory entry into a new class of biologically active compounds, namely N-[1-(1-arylethenyl)]pyridinium salts, which are effective oral antidiabetic agents. Also the reactions with cycloalkenols can be utilized for the stereospecific introduction of other functional groups in these cyclic systems.

It would be interesting to compare the behaviour of chloronium nitrate-pyridine complex and also the reactivities of these compounds as the free pseudohalogens with those of iodonium nitrate and bromonium nitrate discussed before. It is possible that such investigations may throw some light ~~on the~~ effect of complexation with pyridine on the reactivities of these pseudohalogens.

Table 18

In Vivo Hypo/Hyperglycemia*

Structure	Percentage V-Increase (+) or Decrease (-) of Blood Glucose effected by Compound			Summary
	1h	2h	4h	
Threo  $(CH_3)_3C-\underset{I}{CH}-\underset{Py^+NO_3^-}{CH}-CH_3$	3	-7	-10	Inactive
 $I-CH_2-\underset{Py^+NO_3^-}{CH}-O-C_2H_5$	6	7	4	Inactive
	11	11	12	Inactive
	-4	-5	-2	Inactive
	6	7	10	Inactive
	4	2	0	Inactive
	9	7	12	Inactive
 $C_6H_5-\overset{CH_3}{\underset{Py^+NO_3^-}{C}}-CH_2I$	-2	-4	2	Inactive

Continued . . .

Table 18 - Continued

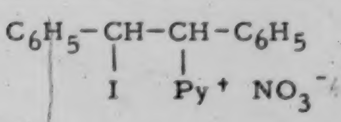
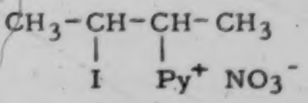
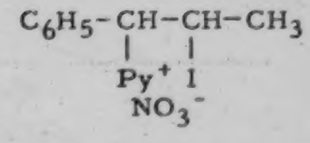
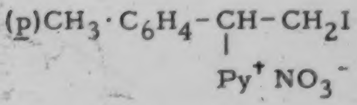
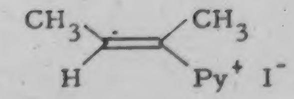
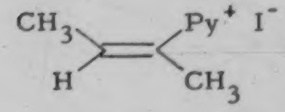
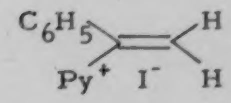
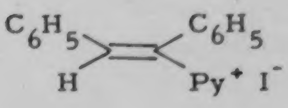
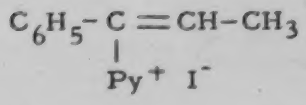
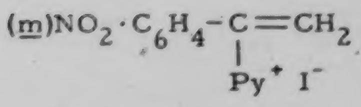
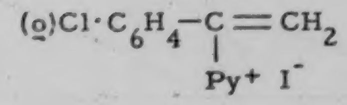
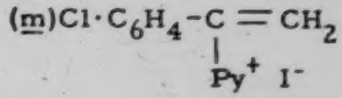
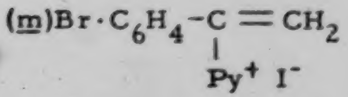
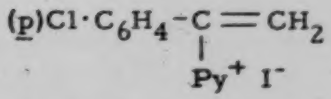
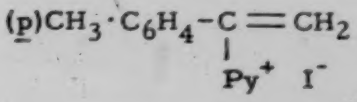
Structure	Percentage V-Increase (+) or Decrease (-) of Blood Glucose effected by Compound			Summary
	1h	2h	4h	
Threo  $C_6H_5-\underset{I}{CH}-\underset{Py^+\ NO_3^-}{CH}-C_6H_5$	18	2	6	Inactive
Erythro  $CH_3-\underset{I}{CH}-\underset{Py^+\ NO_3^-}{CH}-CH_3$	0	- 2	0	Inactive
 $C_6H_5-\underset{\substack{Py^+\\NO_3^-}}{CH}-\underset{I}{CH}-CH_3$	-20	-15	-20	Active
 $(\underline{p})CH_3\cdot C_6H_4-\underset{Py^+\ NO_3^-}{CH}-CH_2I$	-24	-20	-17	Active
	-14	-13	-10	Active
	- 8	-12	-10	Active
	-27	-31	-36	Active
	8	6	- 2	Inactive
 $C_6H_5-\underset{Py^+\ I^-}{C}=CH-CH_3$	-21	-25	-24	Active
 $(\underline{m})NO_2\cdot C_6H_4-\underset{Py^+\ I^-}{C}=CH_2$	- 5	- 8	- 7	Active
 $(\underline{o})Cl\cdot C_6H_4-\underset{Py^+\ I^-}{C}=CH_2$	-18	-20	-20	Active

Table 18 - Continued

Structure	Percentage V-Increase (+) or Decrease (-) of Blood Glucose effected by Compound			Summary
	1h	2h	4h	
 $(\underline{m})Cl\cdot C_6H_4-\underset{\substack{\vert \\ Py^+\ I^-}}{C}=CH_2$	-20	-20	-24	Active
 $(\underline{m})Br\cdot C_6H_4-\underset{\substack{\vert \\ Py^+\ I^-}}{C}=CH_2$	-13	-15	-15	Active
 $(\underline{p})Cl\cdot C_6H_4-\underset{\substack{\vert \\ Py^+\ I^-}}{C}=CH_2$	0	- 3	- 7	Inactive
 $(\underline{p})CH_3\cdot C_6H_4-\underset{\substack{\vert \\ Py^+\ I^-}}{C}=CH_2$	-11	- 8	- 9	Active

$$\text{V percentage} = \frac{\Delta T - \Delta C}{\text{Control Blood glucose value at that hr.}}$$

ΔT = Change from zero time in experimental rats.

ΔC = Change from zero time in control rats.

* These tests were carried out by Dr. R. Cramer of SK & F.

CHAPTER VIII

Experimental

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. The i.r. spectra were recorded on a Perkin-Elmer model 421 Spectrophotometer, and only the principal, sharply defined peaks are reported. The n.m.r. spectra were recorded on a Varian A-60 and A-100 analytical spectrometers. The spectra were measured on approximately 10-15% (w/v) solutions in appropriate deuterated solvents with tetramethylsilane as standard. Line positions are reported in ppm from the reference. Mass spectra were determined on an Associated Electrical Industries MS-9 double focussing high resolution mass spectrometer. The ionization energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for thin layer chromatography.

The g.c. analyses were performed with an Aerograph model A-700 gas chromatograph. The l.c. analyses were made with a Waters Associates model ALC-100 liquid chromatograph. Microanalyses were carried out by Mrs. D. Mahlow of this department.

General Procedure for the Reaction of Iodonium Nitrate with Unsaturated Hydrocarbons.

Silver nitrate, 6.8 g (0.04 mol) was dissolved in a mixture of 50 ml of anhydrous chloroform and 15 ml of anhydrous pyridine. Iodine monochloride, 6.5 g (0.04 mol) in 20 ml of dry chloroform, was added dropwise to the stirred solution. The silver chloride produced was collected and washed with a mixture of 10 ml of chloroform and 10 ml of pyridine. 0.04 mol of the olefin was added all at once to the yellow filtrate. The mixture was stirred at room temperature for 3 h, then poured into an excess of ether and chilled. The resulting precipitate was collected and the filtrate concentrated *in vacuo*. The oil obtained was taken up in 50 ml of ether and washed with 50 ml of 5% cold hydrochloric acid to remove pyridine and then with 25 ml of cold water to remove any remaining pyridinium salt. If the ether solution was colored with iodine, it was washed with 20 ml of 5% sodium thiosulfate solution and then with 20 ml of water. The ether layer was dried ($MgSO_4$) and evaporated *in vacuo*. Further purification of the iodonitrate ester so obtained was effected by distillation under reduced pressure.

The ether insoluble residue after washing several times with ether was extracted with a 50:50 mixture of ethanol:isopropanol and filtered. Ether was added to the filtrate dropwise until the solution turned cloudy. The solution contained in a small beaker was placed in a larger beaker containing a little ether, the large beaker was covered with plastic film and kept in the refrigerator overnight. The resulting precipitate was collected and washed with ether containing a little ethanol and then with ether to afford the iodopyridinium nitrate. In a few instances, when the iodopyridinium salt was difficult to purify and very dark in color (contamination with iodine and tarry materials), the purification was carried out by chromatography on silica gel, eluting with $CHCl_3$, 5% CH_3OH in $CHCl_3$ (v/v), 10% CH_3OH in $CHCl_3$(v/v), and 30% CH_3OH in $CHCl_3$ (v/v), the iodopyridinium salt being collected with the last mixture of solvents.

The spectral and analytical data for the iodonitrate esters and iodopyridinium nitrates obtained from different olefins are summarized in Tables 19-22.

General Procedure for the Zinc-Copper Couple Reduction.

The iodonitrate ester (0.006 mol) was added dropwise to a stirred mixture of 1.5 g of zinc-copper couple (Alfa Inorganics) and 25 ml of glacial acetic acid at room temperature and left stirring overnight. Then, the solid was filtered off and washed with a small amount of ether. The liquid was poured into a mixture of ether and water and solid sodium bicarbonate was added in portions until the solution was completely neutralized. The ether layer was removed and the aqueous layer extracted with more ether. The combined either extracts were dried ($MgSO_4$) and the solvent removed in vacuo. The resulting liquid showed no covalent nitrate absorption in the i.r. spectrum but the presence of hydroxy group. The product was reduced without further purification with excess of lithium aluninum hydride in ether and the resulting alcohols identified by compariosn of their g.c. retention times and i.r. and n.m.r. spectra with those of authentic samples.

General Procedure for the Reaction of Iodonium Nitrate with Terminal Alkynes.

The procedure was similar to that described above. Addition of ether to the reaction mixture resulted in the precipitation of an equivalent amount of pyridinium nitrate which was collected. The remaining solution was concentrated *in vacuo* and the residual oil distilled.

General Procedure for the Preparation of N-[1-(1-Aryl)ethenyl]-Pyridinium Iodides from Styrenes.

Iodonium nitrate (0.04 mol) was prepared in 60 ml of chloroform and 25 ml of pyridine. The styrene (0.04 mol) was added all at once to the stirred solution. The mixture was stirred at room temperature for 3 to $3\frac{1}{2}$ h and then poured into a mixture of water and ether. The aqueous layer was separated, washed several times with ether and the ether discarded. A control experiment with styrene showed that the water soluble material was a mixture of uneliminated pyridinium salt, eliminated pyridinium salt and pyridinium nitrate which were not separable by usual purification procedures. Therefore the aqueous solution was treated with approximately 8 g of solid potassium carbonate and extracted several times with ether and the ether discarded. The solution was adjusted to pH=7 with dilute nitric acid and evaporated to dryness *in vacuo*. Ether was added to the ethanol solution of the residue till the solution turned cloudy. Crystallization by the method described before gave the *N-[1-(1-aryl)ethenyl]-pyridinium iodide*.

The n.m.r. data for the N-[1-(1-aryl)ethenyl]pyridinium iodides thus prepared are summarized in Table 23.

Addition of Iodonium Nitrate to D-Glucal Triacetate in Chloroform-Pyridine.

To a solution of iodonium nitrate (0.02 mol) in 35 ml of chloroform and 12.5 ml of pyridine was added 4.9 (0.018 mol) of D-glucal triacetate. The mixture was stirred at room temperature for 3 h; then poured into an excess of ether and chilled. The resulting oily residue was collected. Evaporation of the filtrate in vacuo did not give any identifiable material.

The ether insoluble residue after washing several times with ether was extracted with hot chloroform. The residue was extracted with cold methanol and filtered. Crystallization was effected by the addition of ether whereupon 2.85 g (29%) of N-[2-(3-iodo-4,5,7-triacetoxy)tetrahydropyranosyl]pyridinium nitrate 42, m.p. 164-166° was obtained.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 8.4-9.4 (m, 5H, pyridine hydrogens); 6.73 (d, 1H, anomeric hydrogen H^1, $J_{1,2}$= 10 Hz); 5.62 (q, 1H, H^4, $J_{3,4}$=10 Hz, $J_{4,5}$=9.5 Hz); 5.21 (t, 1H, H^5, $J_{4,5}$=$J_{5,6}$= 9.5 Hz); 4.89 (t, 1H, H^3, $J_{2,3}$=$J_{3,4}$=10 Hz); 4.4 (m, 1H, H^6); 4.19 (m, 2H, $-CH_2-O$); 2.0-2.98 (3 s, 9H, 3 CH_3COO).

The i.r. spectrum: $\nu_{max.}$ (KBr disc): 1745 ($>$=O); 1630 cm^{-1} (ONO_2^-).

The chloroform solution was concentrated in vacuo and chromatographed on florisil and eluted with $CHCl_3$, 5% CH_3OH in in $CHCl_3$ (v/v), 10% CH_3OH in $CHCl_3$ (v/v), and 15% CH_3OH in $CHCl_3$ (v/v). Evaporation of the last fraction gave 43 and 44, 2.7 g (27%).

The n.m.r. spectrum: δ_{TMS} $(CD_3)_2SO$: 6.69 (d, anomeric hydrogen, J=10 Hz); 6.56 (d, anomeric hydrogen, J=6 Hz).

In another run, the chloroform solution was concentrated *in vacuo*. Crystallization of the oily residue from ethanol:ether gave 3 g (30%) of **42**.

Reaction of Iodonium Nitrate with 2,3-Dimethyl-1,3-butadiene in Chloroform-Pyridine.

To a solution of iodonium nitrate (0.04 mol) in 60 ml of chloroform and 25 ml of pyridine was added 3.28 (0.04 mol) of 2,3-dimethyl-1,3-butadiene all at once. The mixture was stirred at room temperature for 3 h; then poured into an excess of ether and chilled. The resulting precipitate was collected. Evaporation of the filtrate *in vacuo* did not give any identifiable material.

The ether insoluble residue after washing several times with ether was extracted with ethanol at room temperature and filtered. Ether was added dropwise to the filtrate till it turned cloudy. Crystallization by the method discussed before gave 8.4 g (60%) of N-[3-(4-iodo-2,3-dimethyl)butenyl]pyridinium nitrate **55**. m.p. 106-108°.

Anal. Calcd. for $C_{11}H_{15}N_2O_3I$: C, 37.73; H, 4.32; N, 8.00. Found: C, 37.70; H, 4.03; N, 7.91.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 1.67 (s, 3H, $CH_3\text{-}C{=}C$); 2.03 (s, 3H, $CH_3\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{+}{N}\lessgtr$); 4.3 (s, 2H, $\text{-}CH_2I$); 5.28 (s, 1H, one olefinic hydrogen); 5.41 (m, 1H, other olefinic hydrogen); 8.2-9.3 (m, 5H, pyridine hydrogens).

The ethanol insoluble residue was extracted with hot methanol and filtered. Addition of ether and filtration gave 0.8 g (5.5%) of N,N'-[1,4-(2,3-dimethylbut-2-enyl)]dipyridinium dinitrate **56**. m.p. 261-263° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_4O_6$: C, 52.97; H, 5.49; N, 15.38. Found: C, 52.43; H, 5.51; N, 15.33.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 1.82 (s, 6H, 2 $-CH_3$); 5.4 (s, 4H, $-CH_2-\overset{+}{N}\Big\langle$); 7.9-8.8 (m, 10 H, Py).

General Procedure for the Reaction of Iodonium Nitrate with Phenols and Anilines.

The procedure was similar to that explained before. Addition of the reaction mixture to an excess of ether resulted in the precipitation of an equivalent amount of pyridinium nitrate which was collected. The filtrate was concentrated *in vacuo* and the residual oil taken up in ether. The ether extract was washed with water, sodium thiosulfate solution and then with water. Evaporation *in vacuo* after drying ($MgSO_4$) gave the iodinated compound. Purification was effected either by crystallization from a suitable solvent or chromatography on florisil.

The analytical and spectral data for the iodinated compounds thus prepared are summarized in Tables 24 and 25.

General Procedure for the Reaction of Iodonium Nitrate with Unsaturated Alcohols.

The procedure in chloroform-pyridine was similar to that discussed before. When the reactions were carried out in chloroform-*sym*-collidine the following procedure was adopted. The reaction mixture was added to sufficient ether to precipitate the collidinium salt. The precipitate was collected and the ethereal layer was washed several times successively with (a) cold hydrochloric acid (5%) saturated with sodium chloride, (b) saturated aqueous sodium chloride, (c) sodium bicarbonate (5%) saturated with sodium chloride until neutral, and finally (d) saturated sodium chloride solution containing sodium thiosulfate. The ether layer was dried ($MgSO_4$) and concentrated in vacuo. The residual oil was distilled under reduced pressure.

The iodopyridinium salts were purified by the crystallization procedure described before. The analytical and spectral data on the products thus obtained are summarized in Tables 26-30.

Base Catalyzed Cyclization of 1-Iodo-4-hydroxy-4,4-pentamethylenebut-2-yl Nitrate.

To a stirred solution of 7.1 g (0.0215 mol) of 1-iodo-4-hydroxy-4,4-pentamethylenebut-2-yl nitrate in 50 ml of ether was added 2.25 g (0.04 mol) of powdered potassium hydroxide. The mixture was stirred at room temperature overnight and then filtered. The ether solution was washed with 25 ml portions of water twice and dried ($MgSO_4$). Removal of the ether in vacuo gave 3.8 g (88%) of 5,5-pentamethylenetetrahydrofuran-3-yl nitrate 103, which was purified by distillation under reduced pressure. b.p. 66-67°/0.07 mm.

Anal. Calcd. for $C_9H_{15}NO_4$: molecular weight 201.1001 C, 53.72; H, 7.46; N, 6.97. Found: M (mass spectrum), 201.0995. C, 53.97; H, 7.43; N, 6.82.

The n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 1.57 (broad s, 10H, cyclohexane ring hydrogens); 1.9-2.15 (m, 2H, $-CH_2-$); 4.7 (m, 2H, $-CH_2-O$); 5.5 (m, 1H, $-CH-ONO_2$).

The i.r. spectrum: $\nu_{max.}$ (liquid film): 1630, 1275 cm^{-1} ($-ONO_2$).

Addition of Iodonium Nitrate to Pent-4-en-1-ol in Chloroform-Pyridine.

To a solution of iodonium nitrate (0.02 mol) in 30 ml of chloroform and 12.5 ml of pyridine was added 1.55 g (0.018 mol) of pent-4-en-1-ol, the mixture stirred at room temperature for 3 h and the then poured into an excess of ether and chilled. The precipitated pyridinium nitrate was collected and the filtrate concentrated *in vacuo*. The residual oil was taken up in ether and washed successively with 40 ml of cold 5% hydrochloric acid, 25 ml of water, 25 ml of 5% sodium thiosulfate solution and finally with 25 ml of water. The ether layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residual oil was chromatographed on 75 g of florisil and eluted with petroleum ether: chloroform (9:1) and then with chloroform:methanol (9:1). Evaporation of the first fraction gave 2.29 g (60%) of 2-iodomethyltetrahydrofuran **105**.

The n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 3.25 (d, 2H, $-CH_2-I$, J=6 Hz); 1.5-2.3 (m, 4H, 2 $-CH_2-$); 3.6-4.1 (m, 3H, -CH-O, $-CH_2-O$).

Evaporation of the second fraction gave a mixture of 5-hydroxy-1-iodopent-2-yl nitrate **106** and 5-hydroxy-2-iodopent-1-yl nitrate **107**, 0.3 g (6%).

General Procedure for the Reaction of Iodonium Nitrate with 2-Allylphenols in Chloroform-Pyridine.

The reaction was carried out by the general procedure described before. The oil obtained on evaporation of the dried ($MgSO_4$) ether solution was chromatographed on florisil and eluted with hexane: benzene (85:15) and (1:1). Evaporation of the first fraction gave the cyclic ether and evaporation of the second fraction gave the iodonitrate ester:

Addition of Iodonium Nitrate to Hex-5-en-1-ol in Chloroform-Pyridine.

The reaction was carried out by the general procedure described before. The oil obtained on evaporation of the dried ($MgSO_4$) ether solution was chromatographed on florisil and eluted with petroleum ether:chloroform (1:1) and then with chloroform:methanol (9:1). Evaporation of the first fraction gave 0.7 g (17%) of 2-iodomethyltetrahydropyran **117**.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 3.23 (s, 2H, $-CH_2-I$); 0.8-2.5 (m, 6H, 3 $-CH_2-$); 3.1-3.7 (m, 2H, $-CH_2-O$); 3.9-4.25 (m, 1H, -CH-O).

Evaporation of the second fraction gave 1.115 g (21%) of 6-hydroxy-1-iodohexyl nitrate **113**.

The ether insoluble residue was extracted with ethanol and a small amount of ether added. The precipitated pyridinium nitrate was collected and more ether added to the filtrate. The resulting oil was separated by decantation and the excess solvents removed *in vacuo* to afford 2.6 g (39%) of N-[2-(6-hydroxy-1-iodohexyl)]pyridinium nitrate **114** as an oil.

Addition of Iodonium Nitrate to 4-Pentenoic Acid in Chloroform-Pyridine.

The addition was carried out as described before. Thus reaction of iodonium nitrate (0.04 mol) in 60 ml of chloroform and 25 ml of pyridine with 3.6 g (0.036 mol) of 4-pentenoic acid and work-up by the usual procedure gave 4.9 g (60%) of 5-iodomethylbutyrolactone, **131**. Purification was effected by chromatography on florisil and elution with chloroform.

Anal. Calcd. for $C_5H_7O_2I$ (mol. wt. 225.9491): C, 26.56; H, 3.10; I, 56.2. Found: (225.9486, mass spectrum), C, 27.01; H, 3.18; I, 56.28.

The n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 1.7-2.8 (m, 4H, 2 $-CH_2-$); 3.4 (t, 2H, $-CH_2I$, J=4 Hz, 6.5 Hz); 4.6 (m, 1H, -CH-O).

The i.r. spectrum: ν_{max} (liquid film): 1775 cm^{-1} (>C=O).

Endo-cis-5-Norbornene-2,3-dimethanol 118.

32.8 g (0.2 mol) of endo-cis-5-Norbornene-2,3-dicarboxylic anhydride was esterified by refluxing in 175 ml of methanol in the presence of a catalytic amount of concentrated sulfuric acid for $2\frac{1}{2}$ days. Work-up by the usual procedure gave 38.2 g (91%) of endo-cis-dimethyl-5-norbornene-2,3-dicarboxylate. b.p. 104°/0.5 mm.

The n.m.r. spectrum: δ_{TMS} $(CDCl_3)$: 6.23 (t, 2H, H^5, H^6); 3.6 (s, 6H, 2 $-CH_3$); 3.3 (d, 2H, H^2, H^3, $J_{1,6}$=1.5 Hz); 3.2 (m, 2H, H^1, H^4); 1.4 (m, 2H, H^7, $H^{7'}$).

Reduction of 21.0 g (0.1 mol) of endo-cis-dimethyl-5-norbornene-2,3-dicarboxylate with 4.56 g (0.12 mol) of lithium aluminum hydride in 100 ml of refluxing tetrahydrofuran by a literature procedure[165] gave 10 g (65%) of endo-cis-5-norbornene-2,3-dimethanol 118A. m.p. 84-85° (lit., m.p. 86°).

The n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 6.0 (t, 2H, H^5, H^6); 4.53 (s, 2H, 2 -OH); 3.5 (m, 4H, 2 $-CH_2-O$); 2.77 (m, 2H, H^1, H^4); 2.5 (m, 2H, H^2, H^3); 1.4 (m, 2H, H^7, $H^{7'}$).

Similarly reduction of the diester with lithium aluminum deuteride gave endo-cis-5-norbornene-2,3-dimethanol-d_4, 118B (55%). m.p. 85°.

The n.m.r. spectrum: δ_{TMS} (CDCl$_3$): 6.0 (t, 2H, H^5, H^6); 4.27 (s, 2H, 2 -OH); 2.77 (m, 2H, H^1, H^4); 2.5 (broad singlet, 2H, H^2, H^3); 1.4 (m, 2H, H^7, H$^{7'}$).

Addition of Iodonium Nitrate to endo-cis-5-Norbornene-2,3-dimethanol in Chloforom-Pyridine.

Reaction of iodonium nitrate (0.03 mol) in 40 ml of chloroform and 20 ml of pyridine with 4.16 g (0.027 mol) of endo-cis-5-norbornene-2,3-dimethanol at room temperature for $2\frac{1}{2}$ h and work-up by the usual procedure gave the cyclic ether 121A. Yield 5.58 g (74%). Purification was effected by recrystallization from ether-hexane. m.p. 54.5-55.5°.

Anal. Calcd. for $C_9H_{13}O_2I$ (mol. wt. 279.9961): C, 38.56; H, 4.64. Found: (279.9971, mass spectrum), C, 37.87; H, 4.68.

The n.m.r. spectrum: δ_{TMS} (CDCl$_3$): See text.

The i.r. spectrum: ν_{max} (CHCl$_3$): 3620, 3450 cm^{-1} (-OH).

Similarly reaction of endo-cis-5-norbornene-2,3-dimethanol-d$_4$ with iodonium nitrate gave 121B (70%).

Trans-5-Norbornene-2,3-dimethanol, 120.

Diels-Alder condensation between cyclopentadiene (14 ml) and 17.28 g (0.12 mol) of dimethyl fumarate in 200 ml of benzene at 5°C for 24 h gave 22.8 g (91%) of trans-dimethyl-5-norbornene-2,3-dicarboxylate. b.p. 90-91°/0.04 mm. m.p. 29-30°.

The n.m.r. spectrum: δ_{TMS} (CDCl$_3$): 6.2 (m, 2H, H^5, H^6); 3.37 (m, 2H, H^1, H^4); 2.7, 3.33 (m, 2H, H^2, H^3); 1.53 (m, 2H, H^7, H$^{7'}$), 3.63, 3.73 (2s, 6H, 2 -CH$_3$).

Reduction of trans-dimethyl-5-norbornene-2,3-dicarboxylate, 5.0 g (0.0238 mol) with 1.5 g of lithium aluminum hydride in

75 ml of refluxing tetrhydrofuran by the procedure described before gave 2.7 g (72.5%) of *trans*-5-norbornene-2,3-dimethanol. b.p. 120-121°/1 mm (lit., b.p. 132-136°/3 mm)[165].

The n.m.r. spectrum: δ_{TMS}(CDCl$_3$): 1.1-2.1 (m, 4H, H^2, H^3, H^7, H$^{7'}$); 2.6-4.1 (m, 8H, 2 CH$_2$-OH, H^1, H^4); 6.1 (m, 2H, H^5, H^6).

Addition of Iodonium Nitrate to *trans*-5-Norbornene-2,3-dimethanol in Chloroform-Pyridine.

Reaction of iodonium nitrate (0.02 mol) in 30 ml of chloroform and 15 ml of pyridine with 2.772 g (0.018 mol) of *trans*-5-norbornene-2,3-dimethanol at room temperature for 3 h and work-up by the usual procedure gave 4.315 g (86%) of the cyclic ether **123**.

The n.m.r. spectrum: δ_{TMS} (CDCl$_3$): 1.5-2.7 (m, 6H, H^1, H^6, H^5, H^4, H^7, H^{7a}); 3.65 (d, 1H, CH-I, $J_{3,7a}$=2.3 Hz); 4.73 (d, 1H, CH-O, $J_{1,2}$=5 Hz).

The i.r. spectrum: ν_{max} (liquid film): 3400 cm^{-1} (-OH).

Para-Nitrobenzoylation of Cyclic ether **123**.

To a solution of 0.650 g (2.32 mmol) of **123** and 0.237 g (3 mmol) of pyridine in 25 ml of anhydrous benzene was added a solution of 0.431 g (2.32 mmol) of *para*-nitrobenzoyl chloride in 10 ml of anhydrous benzene dropwise and the mixture stirred at room temperature overnight. The precipitated pyridinium chloride was collected and the filtrate washed with 20 ml of 5% sodium bicarbonate solution and then with 20 ml of water. Removal of the solvent *in vacuo* after drying (MgSO$_4$) gave an oil which was crystallized from benzene-hexane to afford 0.7 g (70%) of the *para*-nitrobenzoyl derivative **124**. m.p. 105-105.5°.

Anal. Calcd. for $C_6H_{16}NO_5I$: C, 44.75; H, 3.73; N, 3.26. Found: C, 45.13; H, 3.74; N, 3.29.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.7-2.85 (m, 6H, H^1, H^6, H^5, H^4, H^7, H^{7a}); 3.7 (d, 1H, CH-I, J=2 Hz); 3.8 (d, 2H, $-CH_2-O$, J=2Hz); 4.33 (d, 2H, $-CH_2-O-C=O$, J=8 Hz); 4.8 (d, 1H, CH-O, J=4.5 Hz); 8.35 (m, 4H, aromatic hydrogens).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1735 cm^{-1} ($>C=O$); 1530 cm^{-1} ($-NO_2$).

Exo-*cis*-5-Norbornene-2,3-dimethanol, 119.

Endo-*cis*-5-norbornene-2,3-dicarboxylic anhydride was isomerized to *exo*-*cis*-5-norbornene-2,3-dicarboxylic anhydride thermally according to a literature procedure[165b]. m.p. 140-141° (lit., m.p. 140-142°).

Exo-*cis*-5-norbornene-2,3-dicarboxylic anhydride, 14.6 g (0.089 mol) was esterified in 100 ml of refluxing methanol according to the procedure described before to afford 17.8 g (95%) of *exo*-*cis*-dimethyl-5-norbornene-2,3-dicarboxylate. b.p. 90-91°/0.05 mm.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 6.2 (t, 2H, H^5, H^6); 3.65 (s, 6H, 2-CH_3); 3.1 (m, 2H, H^1, H^4); 2.6 (d, 2H, H^2, H^3); 2.15, 1.5 (m, 2H, H^7, $H^{7'}$).

Exo-*cis*-Dimethyl-5-norbornene-2,3-dicarboxylate, 10 g (0.0476 mol) was reduced with 2.28 g of lithium aluminum hydride in 70 ml of refluxing tetrahydrofuran according to the literature procedure mentioned before to yield 6 g (82%) of *exo*-*cis*-5-norbornene-2,3-dimethanol, 119A. b.p. 112-113°/0.05 mm (lit., b.p. 130-134°/1mm)[165a].

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 6.2 (t, 2H, H^5, H^6); 3.7 (m, 4H, 2 -CH_2-O); 2.55 (m, 2H, H^1, H^4); 1.8 (m, 2H, H^2, H^3); 1.32 (m, 2H, H^7, $H^{7'}$).

Similarly, the diester was reduced with lithium aluminum deuteride to afford *exo*-*cis*-5-norbornene-2,3-dimethanol-d_4, 119B (80%, >95% D).

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 6.2 (t, 2H, H^5, H^6); 2.55 (m, 2H, H^1, H^4); 1.8 (s, 2H, H^2, H^3); 1.32 (m, 2H, H^7, $H^{7'}$); 4.7 (s, 2H, 2 -OH).

Addition of Iodonium Nitrate to *exo*-*cis*-5-Norbornene-2,3-dimethanol in Chloroform-Pyridine.

The reaction was carried out as before with iodonium nitrate (0.02 mol) in chloroform-pyridine and the olefinic alcohol, 2.772 g (0.018 mol). The oil obtained after evaporation of the dried ($MgSO_4$) solution was chromatographed on florisil and eluted with chloroform, chloroform-methanol (19:1) and chloroform-methanol (9:1). Evaporation of the last fraction gave 2.45 g (40%) of the adduct, 126A, which was recrystallized from chloroform-hexane. m.p. 86-88°.

Anal. Calcd. for $C_9H_{14}NO_5I$: C, 31.5; H, 4.08; N, 4.08. Found: C, 31.38; H, 3.99; N, 3.75.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.5-2.6 (m, 6H, H^1, H^6, H^5, H^4, H^{7a}, H^{7b}); 6.2 (s, 2H, 2 -OH); 3.3-4.0 (m, 5H, 2 -CH_2-O, -CH-I); 5.5 (m, 1H, $\underline{CH}$-ONO_2).

The i.r. spectrum: ν_{max} ($CHCl_3$): 3600, 3430 cm^{-1} (-OH); 1637 (O-NO_2).

Similarly reaction of 1.386 g (9 mmol) of exo-cis-5-norbornene-2,3-dimethanol-d_4 with iodonium nitrate (0.01 mol) in chloroform-pyridine and work-up by the method described above gave 1.13 g (36%) of the adduct 126B.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.5-2.6 (m, 6H, H^1, H^6, H^5, H^4, H^{7a}, H^{7b}); 3.82 (t, 1H, -CH-I); 5.5 (m, 1H, -CH-ONO_2).

Anti-7-Norbornenol, 127.

This compound was prepared according to a literature procedure[170]. The n.m.r. spectrum was identical to that reported.

Addition of Iodonium Nitrate to Anti-7-Norbornenol in Chloroform-Pyridine.

The reaction was carried out according to the general procedure. Thus reaction of iodonium nitrate (0.01 mol) and 0.99 g (0.009 mol) of anti-7-norbornenol gave 2 g (74.3%) of anti-7-hydroxy-exo-3-iodo-endo-norborn-2-yl nitrate 128.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.2-2.5 (m, 4H, 2 -CH_2-); 2.2 (s, 1H, -OH); 2.6 (m, 2H, H^1, H^4); 3.6 (d, 1H, -CH-I, J=3 Hz); 4.8 (m, 1H, -CH-OH); 5.6 (m, 1H, -CH-ONO_2).

The i.r. spectrum: ν_{max} ($CHCl_3$): 3600 cm^{-1} (-OH), 1637, 1275 cm^{-1} (-ONO_2).

Para-Nitrobenzoylation of Adduct 128.

The reaction was carried out as described before. Thus from 1 g (3.344 mmol) of adduct 128 and 0.625 g (3.344 mmol) of para-nitrobenzoyl chloride was formed 0.77 g (51.4%) of anti-7-para-nitrobenzoyloxy-exo-3-iodo-endo-norborn-2-yl nitrate, 129. m.p. 119-120° (benzene-hexane).

Anal. Calcd. for $C_4H_{13}N_2O_7I$: C, 37.5; H, 2.9; N, 6.25. Found: C, 38.06; H, 2.94; N, 5.88.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.45-2.25 (m, 4H, 2 -CH_2-); 2.9 (m, 2H, H^1, H^4); 3.75 (d, 1H, -CH-I, J=3 Hz); 5.6 (m, 2H, $\underline{\mathrm{CH}}$-ONO_2, -$\underline{\mathrm{CH}}$-O-$\mathrm{C}\lessgtr^{\mathrm{O}}$).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1733 cm^{-1} ($>C=O$); 1645 cm^{-1} (-ONO_2); 1525 (-NO_2).

Preparation of Iodonium Nitrate-Pyridine Complex.

Iodonium nitrate (0.04 mol) was prepared in 50 ml of chloroform and 25 ml of pyridine. The solution was poured into an excess of ether and chilled. The resulting precipitate was collected and washed several times with ether. Repeated recrystallization of the solid from anhydrous acetonitrile or acetonitrile-ether gave 11g (79%) of iodonium nitrate-pyridine complex, $\underset{\smile}{134}$ as a crystalline solid. m.p. 128-131° (lit., m.p. 138°)[129].

Anal. Calcd. for $C_{10}H_{10}N_3O_3I$: C, 34.59; H, 2.88; N, 12.1. Found: C, 34.25; H, 3.19; N, 10.56.

Addition of Iodonium Nitrate-Pyridine Complex to (E)-4,4-Dimethylpent-2-ene in Dimethyl Sulfoxide.

A mixture of 3.47 g (0.01 mol) of iodonium nitrate-pyridine complex, 0.98 g (0.01 mol) of (E)-4,4-dimethylpent-2-ene and 20 ml of anhydrous dimethyl sulfoxide was stirred at room temperature for 5 h, and then poured into a mixture of water and ether. The ether layer was removed and the aqueous layer extracted with a small amount of ether. The combined ether extracts were washed successively with 50 ml of water, 40 ml of 10% sodium thiosulfate solution, 50 ml of water, 40 ml of 5% hydrochloric acid and then with 50 ml of water. Drying ($MgSO_4$) and removal of the solvent *in vacuo* gave 1.7g (60%) of *erythro*-3-iodo-4,4-dimethylpent-2-yl nitrate, **135**. b.p. 48.5-50°/3.4 mm.

Addition of Iodonium Nitrate-Pyridine Complex to (*E*)-4,4-Dimethylpent-2-ene in Acetonitrile.

A mixture of 3.47 g (0.01 mol) of iodonium nitrate-pyridine complex, 0.98 g (0.01 mol) of (*E*)-4,4-dimethylpent-2-ene and 20 ml of anhydrous acetonitrile was stirred at room temperature for 3h and then concentrated *in vacuo*. The residue was extracted with ether. The ether extract was washed successively with 20 ml of water, 20 ml of 5% hydrochloric acid and then with 20 ml of water. Drying ($MgSO_4$) and removal of the solvent *in vacuo* gave 2.6 g (91%) of *erythro*-3-iodo-4,4-dimethylpent-2-yl nitrate, **135**.

The ether insoluble residue was extracted with ethanol and crystallization by the procedure described before gave 50 mg of *erythro*-N-[2-(3-iodo-4,4-dimethyl)pentyl]pyridinium nitrate, **137**. m.p. 121-124°.

Addition of Iodonium Nitrate to 3-Allyl-1,1-diethyl-2-thiourea in Chloroform-Pyridine.

To a stirred solution of iodonium nitrate (0.02 mol) in 40 ml of chloroform and 15 ml of pyridine was added 3.49 g (0.02 mol) of 3-allyl-1,1-diethyl-2-thiourea all at once. An exothermic reaction took place and the color changed to dark brown. The mixture was stirred at room temperature for 3 h, then poured into an excess of ether and chilled. The resulting residue was collected, washed several times with ether and extracted with cold methanol, filtered and reprecipitated with ether. The residue was chromatographed on

100 g of silica gel and eluted with benzene-methanol (85:15). Evaporation of the eluate gave an oily residue (3.3 g) which solidified slowly on standing to give 2-diethylamino-5-iodomethyl-2-thiazoline, 133.

Anal. Calcd. for $C_8H_{15}N_2SI$ (Mol. Wt. 298.0001). Found: (298.0003, mass spectrum).

The n.m.r. spectrum: δ_{TMS} $(CD_3)_2SO$: 1.03 (t, 6H, 2 CH_3-CH_2-, J=6.5 Hz); 3.3-4.6 (m, 9H, -CH_2-, -CH_2I, 2 -N-CH_2-, -CH-).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1597-1625 (-C=N-).

Addition of Iodine Azide to Cyclohex-2-en-1-ol.

This reaction was carried out by the procedure of Hassner and co-workers.[106] Thus the reaction of 3.92 g (0.04 mol) of cyclohex-2-en-1-ol with iodine azide generated from 5.2 g (0.08 mol) of sodium azide and 9.8 g (0.06 mol) of iodine monochloride in 70 ml of anhydrous acetonitrile at 0° for 24 h and work-up by the usual procedure gave 9.2 g (86%) of 3-hydroxy-2-iodo-1-azidocyclohexane, 142, as a dark brown oil.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1-2.5 (m, 6H, 3 -CH_2-); 2.85 (s, 1H, -OH); 3.9 (m, 2H, -$\underline{CH}$-OH, -CH-N_3); 4.3 (q, 1H, -CH-I, $J_{1,2}$=9.5 Hz, $J_{2,3}$=2.5 Hz).

The i.r. spectrum: ν_{max} (liquid film); 3425 cm^{-1} (-OH); 2100 cm^{-1} (-N_3).

Addition of Iodine Monochloride to Cyclohex-2-en-1-ol.

To a stirred solution of 8.1 g (0.05 mol) of iodine monochloride in 60 ml of anhydrous acetonitrile at 0° was added a solution of 3.92 g (0.04 mol) of cyclohex-2-en-1-ol in 10 ml of anhydrous acetonitrile and the mixture stirred at 0-5° for 24 h. The solution was added to 50 ml of saturated sodium bisulfite solution and the mixture extracted with 50 ml of ether. Removal of the solvent in vacuo after drying ($MgSO_4$) gave 9.4 g (90%) of the adduct as a dark brown oil.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.2-2.6 (m, 7H, 3 $-CH_2-$, -OH); 3.2-3.8 (m, 3H, -CH-I, -CH-Cl, -CH-OH).

The i.r. spectrum: ν_{max} (liquid film): 3420 cm^{-1} (-OH).

Cyclopent-2-en-1-ol.

This compound was prepared by addition of hydrogen chloride to cyclopentadiene followed by hydrolysis of the cyclopent-2-en-1-yl chloride with aqueous sodium bicarbonate according to a literature procedure. b.p. 24-25°/0.65 mm (lit., b.p. 52°/12 mm)[191].

Cyclohept-2-en-1-ol.

Cycloheptene was brominated with N-bromosuccinimide in refluxing carbon tetrachloride in the presence of a trace of benzoyl peroxide to cyclohept-2-en-1-yl bromide. Yield 48%. b.p. 31°/0.1 mm. (lit., b.p. 59°/5.2 mm)[176].

Hydrolysis of cyclohept-2-en-1-yl bromide with 10% sodium hydroxide gave cyclohept-2-en-1-ol. Yield 89%. b.p. 43-44°/0.05 mm (lit., b.p. 72°/7mm)[176].

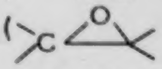
Cyclooct-2-en-1-ol.

This compound was prepared by bromination of cyclooctene with N-bromosuccinimide followed by hydrolysis of the 3-bromocyclooctene with 10% sodium hydroxide. b.p. 46-47°/0.05 mm (lit., b.p. 74°/2 mm)[192].

Treatment of Cyclohept-2-en-1-ol-Iodonium Nitrate Adducts with Potassium Hydroxide in Ether.

A solution of 2.5 g (8.3 mmol) of the adducts in 50 ml of ether was stirred with 0.6 g of powdered potassium hydroxide for 3 h. Work-up according to the procedure described before gave 1 g of cyclohept-2-en-1-one and a small amount of 2,3-epoxycyclohept-1-yl nitrate 146. Separation was achieved by chromatography on florisil and elution with benzene-hexane (50:50). Evaporation of the first fraction gave the epoxy-nitrate.

The n.m.r. spectrum : δ_{TMS} ($CDCl_3$): 0.8-2.5 (m, 8H, 4 -CH_2-); 3.2 (m, 2H, 2 -CH-O); 5.25 (m, 1H, -CH-ONO_2).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1630 cm^{-1}, 1270 cm^{-1} (ONO_2); 1310, 960 cm^{-1} ().

Evaporation of the second fraction gave cyclohept-2-en-1-one, which was identical with an authentic sample.

Para-Nitrobenzoylation of 3-Hydroxy-2-iodo-cycloheptyl Nitrate.

To a solution of 2 g (6.63 mmol) of adducts 143 and 144 and 0.79 g (0.01 mol) of pyridine in 30 ml of anhydrous benzene was added a solution of 1.245 g (0.00663 mol) of para-nitrobenzoyl chloride in 10 ml of benzene dropwise and the mixture stirred for 3 h. Work-up by the usual procedure gave an oil which was crystallized from benzene-hexane to afford 1.5 g (50%) of 3-(para)-nitrobenzoyloxy-2-iodo-cycloheptyl nitrate, 145. m.p. 103-104°.

Anal. Calcd. for $C_{14}H_{15}N_2O_7I$: C, 37.34; H, 3.33; N, 6.22. Found: C, 37.4; H, 3.41; N, 6.25.

The n.m.r. spectrum : δ_{TMS} ($CDCl_3$): 1.7-2.5 (m, 8H, 4 -CH_2-); 4.77 (q, 1H, -CH-I, J=2.5 Hz, 6.5 Hz); 4.96 (m, 1H,

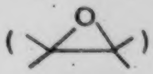
-CH-O); 5.5 (m, 1H, -CH-ONO_2); 8.27 (m, 4H, aromatic hydrogens).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1730 cm^{-1} (>C=O), 1640 (-ONO_2), 1530 (-NO_2).

Treatment of 3-Hydroxy-2-iodocyclooctyl Nitrate with Potassium Hydroxide in Ether.

To a solution of 2 g (6.35 mmol) of 3-hydroxy-2-iodocyclooctyl nitrate in 50 ml of ether was added 0.56 g (0.01 mol) of powdered potassium hydroxide. The mixture was stirred at room temperature for 3 h. Work-up by the usual procedure gave 1 g (84%) of 2,3-epoxycyclooctyl nitrate, 149. Purification was achieved by chromatography on florisil and elution with benzene-hexane (50:50).

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.1-2.4 (m, 10H, 5 -CH_2-); 2.88 (q, 1H, H^3); 3.08 (t, 1H, H^2, J=4 Hz); 5.63 (sextet 1H, -CH-ONO_2, J=5 Hz, 3.33 Hz).

The i.r. spectrum: ν_{max} ($CHCl_3$): 1640 cm^{-1} (ONO_2), 1280 cm^{-1} ().

The mass spectrum: m/e, 141 (M-NO_2); 125 (M-ONO_2).

General Procedure for the Reaction of Iodonium Nitrate with Stereoisomeric Alkenes.

Representative examples of additions to (E)-(Z) pairs of alkenes leading predominantly to iodoalkyl nitrate esters and iodopyridinium nitrate salts respectively are given. Thereafter the results are summarized in Tables 31-34.

Addition of Iodonium Nitrate to (E)-4,4-Dimethylpent-2-ene in the Presence of Pyridine.

The reaction was carried out by the general procedure described before. Thus the reaction of iodonium nitrate (0.04 mol) in 80 ml of chloroform and 25 ml of pyridine with 3.925 g (0.04 mol) of 4,4-dimethylpent-2-ene and work-up by the usual procedure gave 8.7 g (76%) of erythro-3-iodo-4,4-dimethylpent-2-yl nitrate, 135. Purification was effected by distillation under reduced pressure. b.p. 48.5-50°/3.4 mm.

Anal. Calcd. for $C_7H_{14}NO_3I$: C, 29.27; H, 4.88; N, 4.88. Found: C, 28.92; H, 4.90; N, 4.88.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.22 (s, 9H, $-C(CH_3)_3$); 1.52 (d, 3H, $\underline{CH_3}$-CH-ONO_2, J=6.2 Hz); 4.42 (d, 1H, -CH-I, $J_{\underline{CH}I-\underline{CH}ONO_2}$ =2.75 Hz); 4.8 (octet, 1H, -CH-ONO_2, $J_{\underline{CH_3}-\underline{CH}-ONO_2}$ = 6.2 Hz, $J_{\underline{CH}I-\underline{CH}ONO_2}$ = 2.75 Hz).

The i.r. spectrum: ν_{max} (liquid film): 1625, 1270 cm^{-1} ($-ONO_2$).

The ether insoluble residue after washing several times with ether was crystallized from ethanol-isopropanol-ether by the method described before to afford 0.7 g (4.8%) of erythro-N-[2-(3-iodo-4,4-dimethyl)pentyl] pyridinium nitrate, 137. m.p. 120-123°.

Anal. Calcd. for $C_{12}H_{19}N_2O_3I$: C, 39.35; H, 5.19. Found: C, 39.33; H, 5.00.

The n.m.r. spectrum: δ_{TMS}[$(CD_3)_2SO$]: 1.2 (s, 9H, $-C(CH_3)_3$); 1.74 (d, 3H, $-CH_3$, $J_{\underline{CH_3}-\underline{CH}-\overset{+}{N}\lessgtr}$ = 7 Hz); 4.6-5.15 (m, 2H, -CH-I, $-CH-\overset{+}{N}\lessgtr$); 8.2-9.3 (m, 5H, pyridine hydrogens).

The i.r. spectrum: ν_{max} (KBr disc): 1620 cm^{-1} (ONO_2^-).

Addition of Iodonium Nitrate to (*Z*)-4,4-Dimethylpent-2-ene in the Presence of Pyridine.

The reaction of iodonium nitrate (0.04 mol) in 80 ml of chloroform and 25 ml of pyridine with 3.925 g (0.04 mol) of (*Z*)-4,4-dimethylpent-2-ene and work-up by the usual procedure gave 10.59 g (91.5%) of *threo*-3-iodo-4,4-dimethylpent-2-yl nitrate, **156**. b.p. 52-53°/3 mm.

Anal. Calcd. for $C_7H_{14}NO_3I$: C, 29.27; H, 4.88; N, 4.88. Found: C, 29.62; H, 4.88; N, 4.88.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.19 (s, 9H, $-C(CH_3)_3$); 1.53 (d, 3H, $-CH_3$, $J_{\underline{CH}_3-\underline{CH}-ONO_2}$ = 6.15 Hz); 3.99 (d, 1H, -CH-I, $J_{\underline{CH}I-\underline{CH}-ONO_2}$=1.5 Hz); 4.93 (octet, 1H, $-CH-ONO_2$, $J_{\underline{CH}I-\underline{CH}-ONO_2}$=1.5 Hz, $J_{\underline{CH}_3-\underline{CH}-ONO_2}$=6.15 Hz).

The i.r. spectrum: ν_{max} (liquid film): 1625, 1270 cm^{-1} ($-ONO_2$).

From the ether insoluble residue was isolated 0.8 g (5.46%) of *threo*-N-[2-(3-iodo-4,4-dimethyl)pentyl]pyridinium nitrate, **157**. m.p. 82-85°.

Anal. Calcd. for $C_{12}H_{19}N_2O_3I$: C, 39.35; H, 5.19. Found: C, 40.10; H, 5.26.

The n.m.r. spectrum: δ_{TMS}[$(CD_3)_2SO$]: 1.17 (s, 9H, $-C(CH_3)_3$); 1.87 (d, 3H, $-CH_3$, $J_{\underline{CH}_3-\underline{CH}-\overset{+}{N}<}$=6.5 Hz); 4.9-5.4 (m, 2H, -CH-I, $-CH-\overset{+}{N}<$); 8.3-9.4 (m, 5H, pyridine hydrogens).

The i.r. spectrum: ν_{max} (KBr disc): 1620 cm^{-1} (ONO_2^-).

Zinc-Copper Couple Reduction of *Erythro*-3-Iodo-4,4-dimethylpent-2-yl Nitrate, **135**.

The reaction was carried out by the general procedure described before. Thus reduction of 16.5 g (0.0575 mol) of *erythro*-3-iodo-4,4-dimethylpent-2-yl nitrate with 14.3 g of zinc-copper couple in 230 ml of glacial acetic acid at room temperature for 24 h and work-up by the usual procedure gave 4 g (29%) of *erythro*-3-iodo-4,4-dimethylpentan-2-ol, **136**. Purification was effected by chromatography on 120 g of neutral alumina and elution with pentane containing 4% (v/v) of methanol. m.p. 59-60°.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.15 (s, 9H, $-C(CH_3)_3$); 1.28 (d, 3H, $-CH_3$, $J_{\underline{CH}_3-\underline{CH}-OH}$=6 Hz); 1.9 (s, 1H, -OH); 3.11 (octet, 1H, $-\underline{C}H-OH$, $J_{\underline{CH}_3-\underline{CH}-OH}$=6Hz, $J_{\underline{CHI}-\underline{CH}-OH}$=2.9 Hz); 4.58 (d, 1H, -CH-I, $J_{\overline{CHI}-\overline{CH}-OH}$=2.9 Hz).

The i.r. spectrum: ν_{max} ($CHCl_3$): 3540 cm^{-1} (-OH).

Preparation of *E*-2,3-Epoxy-4,4-dimethylpentane from *Erythro*-3-Iodo-4,4-dimethylpentan-2-ol, **136**.

To a stirred solution of 2.4 g (0.01 mol) of *erythro*-3-iodo-4,4-dimethylpentan-2-ol in 80 ml of ether was added 0.85 g (0.015 mol) of powdered potassium hydroxide in small portions. The mixture was stirred at room temperature for 1½ h, filtered, and the residue washed with a small amount of ether. The combined ether extracts were washed with 50 ml of water, dried ($MgSO_4$) and the ether evaporated *in vacuo* at room temperature to afford 0.8 g (70%) of (*E*)-2,3-epoxy-4,4-dimethylpentane, **158**. Purification was effected by distillation under reduced pressure. The sample was identical in physical properties with the authentic epoxide prepared as follows.

Epoxidation of (E)-4,4-Dimethylpent-2-ene with *m*-Chloroperbenzoic Acid.

A mixture of 6.6 g (80% pure, 0.03 mol) of *meta*-chloroperbenzoic acid, 5 g of anhydrous sodium bicarbonate and 80 ml of methylene chloride was cooled in an ice-water bath. 2 g (0.02 mol) of (E)-4,4-dimethylpent-2-ene was added all at once and the mixture stirred at 0° for 3 h. The reaction mixture was kept in the refrigerator overnight, filtered, and the residue washed with a small amount of methylene chloride. The methylene chloride solution was washed with 40 ml portions of 10% potassium carbonate solution twice and then with 40 ml of water, dried ($MgSO_4$) and the solvent evaporated *in vacuo* at room temperature to afford 2 g of (E)-2,3-epoxy-4,4-dimethylpentane, **158**. Purification was effected by distillation. Yield (pure **158**) 1.5 g (68%). b.p. 102-103°/700 mm.

Anal. Calcd. for $C_7H_{14}O$: $(M\text{-}CH_3)$, 99.0810 . Found: (99.0811, mass spectrum).

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 0.90 (s, 9H, $-C(CH_3)_3$); 1.25 (d, 3H, $-CH_3$, $J_{\underline{CH}_3\text{-}\underline{CH}\text{-}O}=5.1$ Hz); 2.35 (d, 1H, $-O\text{-}\underline{CH}\text{-}C(CH_3)_3$, $J_{\text{-}\underline{CH}\text{-}\underline{CH}\text{-}}=2.2$ Hz); 2.79 (octet, 1H, $-O\text{-}\underline{CH}\text{-}CH_3$, $J_{\text{-}\underline{CH}\text{-}\underline{CH}_3}=5.1$ Hz, $J_{\text{-}\underline{CH}\text{-}\underline{CH}\text{-}}=2.2$ Hz).

The i.r. spectrum: ν_{max} (liquid film): 1250, 907, 760 cm^{-1} ( ); 3010 cm^{-1} ($\underset{H}{\overset{|}{-C}}\text{-O}$).

Zinc-Copper Couple Reduction of *Threo*-3-Iodo-4,4-dimethylpent-2-yl Nitrate, **156**.

Reduction of 12.1 g (0.04216 mol) of *threo*-3-iodo-4,4-dimethylpent-2-yl nitrate with 13.1 g of zinc-copper couple in 170 ml of glacial acetic acid and 100 ml of pentane at room temperature for

48 h and work-up by the procedure described before gave 4.2 g (41%) of *threo*-3-iodo-4,4-dimethylpentan-2-ol, **159**. Purification was effected by chromatography on 120 g of neutral alumina and elution with pentane containing 4% (v/v) of methanol. The material was a low melting solid.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.15 (s, 9H, $-C(CH_3)_3$); 1.2 (d, overlapped by *t*-Bu, 3H, $-CH_3$); 1.66 (s, 1H, -OH); 3.11 (m, 1H, -CH-OH); 4.13 (d, 1H, -CH-I, $J_{-CH-CH-}$ = 1.5 Hz).

The i.r. spectrum: ν_{max} ($CHCl_3$): 3430 cm^{-1} (-OH).

Preparation of (*Z*)-2,3-Epoxy-4,4-dimethylpentane, from *Threo*-3-Iodo-4,4-dimethylpentan-2-ol, **159**.

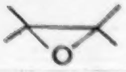
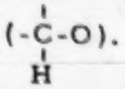
Treatment of *threo*-3-iodo-4,4-dimethylpentan-2-ol in ether with potassium hydroxide according to the conditions described for **158** above gave a mixture of (*Z*)-2,3-epoxy-4,4-dimethylpentane, **160** and a ketonic fraction. Combined yield, 0.5 g (44%). The epoxide was identical with an authentic sample (see below). The ketone was shown to be 4,4-dimethylpentan-2-one by comparison of its n.m.r. and i.r. spectra and g.c. retention time with those of an authentic sample.

Epoxidation of (*Z*)-4,4-Dimethylpent-2-ene with *m*-Chloroperbenzoic Acid.

An authentic sample of (*Z*)-2,3-epoxy-4,4-dimethylpentane, **160** was prepared from (*Z*)-4,4-dimethylpent-2-ene by treatment with *m*-chloroperbenzoic acid according to the conditions described above for **158**. Distillation gave the pure epoxy compound (68% yield). b.p. 110-111.5°/700 mm.

Anal. Calcd. for $C_7H_{14}O$: $(M-CH_3)$, 99.0810. Found: (99.0811, mass spectrum).

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.04 (s, 9H, $-C(CH_3)_3$); 1.43 (d, 3H, $-CH_3$, $J_{\underline{CH}_3-\underline{CH}-O}=5.7$ Hz); 2.6 (d, 1H, $-O-\underline{CH}-C(CH_3)_3$, $J_{-\underline{CH}-\underline{CH}-}=4.5$ Hz); 2.97 (octet, 1H, $-O-\underline{CH}-CH_3$, $J_{-\underline{CH}-\underline{CH}_3}=5.7$ Hz, $J_{-\underline{CH}-\underline{CH}-}=4.5$ Hz).

The i.r. spectrum: ν_{max} (liquid film): 1260, 900 cm^{-1} (); 3010 cm^{-1}  $(-\underset{H}{\overset{|}{C}}-O)$.

General Procedure for the Addition of Iodonium Nitrate to But-2-enes in the Presence of Pyridine.

A solution of iodonium nitrate (0.08 mol) in 150 ml of chloroform and 50 ml of pyridine was cooled in an ice-water bath. But-2-ene gas was passed through the stirred solution in a slow stream for $1\frac{1}{2}$ h. The mixture was stirred at 0° for an additional $1\frac{1}{2}$ h and then worked up by the usual procedure.

The analytical and spectral data for the iodonitrate esters and iodopyridinium salts are included in Tables 31-34.

Base Catalyzed Elimination of Hydrogen Iodide from *Erythro*-N-[2-(3-Iodobutyl)]pyridinium Nitrate, **164**.

14 g (0.0432 mol) of *erythro*-N-[2-(3-iodobutyl)]pyridinium nitrate was dissolved in 70 ml of methanol and 3 g (0.0555 mol) of sodium methoxide added. The mixture was stirred at 50° for 20 h, cooled and the precipitated salts were collected. The filtrate was poured into an excess of ether, chilled and the resulting precipitate collected. Recrystallization from ethanol-isopropanol-ether gave 9.5 g (84%) of (E)-N-[2-(2-butenyl)]pyridinium iodide, **165**. m.p. 138-139°.

Anal. Calcd. for $C_9H_{12}NI$: C, 41.38; H, 4.60; N, 5.36. Found: C, 40.82; H, 4.68; N, 5.34.

The n.m.r. spectrum: δ_{TMS} $[(CD_3)_2SO]$: 1.9 (2q, 3H, $\underline{CH}_3\text{-}CH$, $J_{\underline{CH}_3\text{-}\underline{CH}=}$ = 7.3 Hz; $J_{\underline{CH}_3\text{-}C=C\text{-}CH_3}$ = 1.3 Hz); 2.36 (quint, 3H, $CH_3\text{-}\overset{\|}{C}\text{-}\overset{+}{N}\leqq$, $J_{\underline{CH}_3\text{-}C=C\text{-}\underline{CH}_3}$ • $J_{\underline{CH}=C\text{-}\underline{CH}_3}$ = 1.3 Hz); 6.16 (octet, 1H, $CH_3\text{-}\underline{CH}=$, $J_{\underline{CH}=C\text{-}\underline{CH}_3}$ = 1.3 Hz, $J_{\underline{CH}_3\text{-}\underline{CH}=}$ = 7.3 Hz); 8.2-9.33 (m, 5H, pyridine hydrogens).

Base Catalyzed Elimination of Hydrogen Iodide from *Threo*-N-[2-(3-Iodobutyl)]pyridinium Nitrate, 168.

Treatment of *threo*-N-[2-(3-iodobutyl)]pyridinium nitrate with a slight excess of sodium methoxide in refluxing methanol for 48 h and work-up by the method described above afforded (Z)-N-[2-(2-butenyl)]pyridinium iodide, 169. Yield 87%. m.p. 182-184°.

Anal. Calcd. for $C_9H_{12}NI$: C, 41.38; H, 4.60; N, 5.36. Found: C, 39.22; H, 4.58; N, 5.14.

The n.m.r. spectrum: δ_{TMS} $[(CD_3)_2SO]$: 1.47 (2q, 3H, $\underline{CH}_3\text{-}CH$, $J_{\underline{CH}_3\text{-}C=C\text{-}\underline{CH}_3}$ = 1.7 Hz, $J_{\underline{CH}_3\text{-}\underline{CH}=}$ = 7 Hz); 2.38 (quint, 3H, $\underline{CH}_3\text{-}\overset{\|}{C}\text{-}\overset{+}{N}\leqq$, $J_{\underline{CH}_3\text{-}C=\underline{CH}\text{-}}$ = $J_{\underline{CH}_3\text{-}C=C\text{-}\underline{CH}_3}$ = 1.7 Hz); 6.14 (m, 1H, -CH, $J_{\underline{CH}_3\text{-}\underline{CH}=}$ = 7 Hz, $J_{\underline{CH}_3\text{-}C=\underline{CH}\text{-}}$ = 1.5 Hz); 8.2-9.15 (m, 5H, pyridine hydrogens).

Determination of Ratio of *Threo*-N-[2-(3-Iodopentyl)] and *Threo*-N-[3-(2-Iodopentyl)]pyridinium Nitrates, 26 and 27.

A mixture of 7 g (0.0207 mol) of the isomeric iodopyridinium nitrates, 26 and 27, 1.8 g (0.033 mol) of sodium methoxide and 50 ml of methanol was refluxed for 48 h. Work-up by the method described above gave 3.5 g (61.5%) of (Z)-N-[2-(2-pentenyl)] and (Z)-N-[3-(2-pentenyl)]pyridinium iodides, 172 and 173 respectively. m.p. 90-95°.

Anal. Calcd. for $C_{10}H_{14}NI$: C, 43.64; H, 5.09; N, 5.09. Found: C, 42.2; H, 4.97; N, 5.12.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 0.98 (q, 3H, $\underline{CH}_3\text{-}CH_2\text{-}$, J=7.5 Hz); 1.44 (d, further split by long range coupling, 0.81 H, $\underline{CH}_3\text{-}CH\text{=}$, $J_{\underline{CH}_3\text{-}\underline{CH}=}$ =7 Hz); 1.74 (quint, 1.46H, $\text{-}\underline{CH}_2\text{-}CH$, $J_{\underline{CH}_3\text{-}\underline{CH}_2\text{-}} = J_{\text{-}\underline{CH}_2\text{-}\underline{CH}=}$ =7.5 Hz); 2.34 (s, further split by long range coupling, 2.19H, $CH_3\text{-}\overset{\|}{C}\text{-}\overset{+}{N}\lessgtr$); 2.68 (m, 0.54H, $\text{-}CH_2\text{-}\overset{\|}{C}\text{-}\overset{+}{N}\lessgtr$); 6.04 (m, 1H, -CH=); 8.25-9.3 (m, 5H, pyridine hydrogens).

Proof of Regiochemistry of Addition of Iodonium Nitrate to (E)-3-Methylpent-2-ene by Base Catalyzed Elimination of Hydrogen Iodide from Threo-N-[3-(2-Iodo-3-methyl)pentyl]pyridinium Nitrate, 195.

A mixture of 1.6 g (4.5 mmol) of threo-N-[3-(2-iodo-3-methyl)pentyl]pyridnium nitrate, 1 g (0.019 mol) of sodium methoxide and 40 ml of methanol was refluxed for 48 h, cooled, poured into an excess of ether and chilled. The resulting precipitate was collected and recrystallization from ethanol-ether gave 0.5 g (38%) of N-[3-(3-methyl)pent-1-enyl]pyridinium iodide, 196. m.p. 72-75°.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 0.75 (t, 3H, $\underline{CH}_3\text{-}CH_2\text{-}$, J=7.5 Hz); 1.87 (s, 3H, $CH_3\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{+}{N}\lessgtr$); 2.27 (q, 2H, $\text{-}\underline{CH}_2\text{-}CH_3$, J=7.5 Hz); 5.37-5.70 (q, 2H, CH_2); 6.1-6.57 (q, 1H, -CH); 8.1-9.31 (m, 5H, pyridine hydrogens).

Base Catalyzed Elimination of Hydrogen Iodide from Erythro and Threo-N-[1-(2-Iodo-1,2-diphenyl)ethyl]pyridinium Nitrates.

The iodopyridinium nitrate was stirred with an excess of potassium carbonate in water overnight. The resulting yellow precipitate was collected, washed several times with water and finally with a small amount of ice-cold acetone. Recrystallization from acetone gave pure N-(1,2-diphenylethenyl)pyridinium iodide as yellow needles.

The analytical data for the (Z) and (E) isomers thus prepared are included in Table 32.

(Z)-β-Deuterostyrene.

This olefin was prepared by the method of Hassner and co-workers. It contained > 95% D (by n.m.r. and mass spectroscopy).

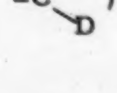
Addition of Iodonium Nitrate to (Z)-β-Deuterostyrene in the Presence of Pyridine.

To a solution of iodonium nitrate (0.02 mol) in 30 ml of chloroform and 12.5 ml of pyridine was added 2.1 g (0.02 mol) of (Z)-β-deuterostyrene all at once. The mixture was stirred at room temperature for $3\frac{1}{2}$ h and then poured into a mixture of water and ether. Work-up of the ethereal layer by the method described before gave a trace of threo-2-deutero-2-iodo-1-phenylethyl nitrate, 206.

The n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 3.47 (d, further split by H-D coupling, 1H, -CH-D, $J_{CH-CH-D}$=8 Hz); 5.93 (d, 1H, -CH-ONO_2, $J_{CH-CH-D}$=8 Hz); 7.4 (m, 5H, Ph).

The aqueous solution was treated with 4 g of solid potassium carbonate and extracted several times with ether, and the ether discarded. The solution was adjusted to pH=7 with dilute nitric acid and evaporated to dryness in vacuo. Extraction of the residue with ethanol and crystallization by the usual procedure gave 2.0 g (32%) of (Z)-N-[1-(2-deutero-1-phenyl)ethenyl]pyridinium iodide, 208.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 6.43 (s, 1H,



$=C\begin{smallmatrix}H\\D\end{smallmatrix}$); 7.45 (m, 5H, Ph); 8.17-9.27 (m, 5H, pyridine hydrogens).

General Procedure for the Addition of Bromonium Nitrate to Unsaturated Substrates.

Silver nitrate, 6.8 g (0.04 mol) was dissolved in a mixture of 30 ml of chloroform and 15 ml of reagent grade pyridine. The solution was cooled in an ice-water bath and bromine, 6.4 g (0.04 mol), in 15 ml of chloroform, was added dropwise to the stirred solution. The silver bromide produced was collected and washed with a mixture of 10 ml of chloroform and 10 ml of pyridine. To the clear light yellow filtrate at 0°, 0.04 mol of the olefin was added all at once. The mixture was stirred at 0° for 3-4 h and then poured into an excess of ether and chilled. The resulting oil or precipitate was collected and the ether solution concentrated *in vacuo*. The residual oil was extracted with ether, washed with 50 ml of cold 5% hydrochloric acid and then with 50 ml of water. Concentration of the solution, after drying ($MgSO_4$), *in vacuo* gave the bromonitrate ester, which was purified by distillation under reduced pressure.

The ether insoluble residue, after washing several times with ether, was extracted with ethanol and filtered. Crystallization was effected by the addition of ether. The product thus obtained is the bromopyridinium nitrate.

In a few instances, addition of the reaction mixture to ether did not give any oil or precipitate. In those cases, the solution was concentrated *in vacuo* and the resulting oil extracted several times with ether. After that work-up was accomplished by the procedure described before.

The analytical and spectral data for the bromonitrate esters and bromopyridinium nitrate salts thus obtained are summarized in

Tables 35-38.

Addition of Bromonium Nitrate to 2,3-Dimethyl-1,3-butadiene in the Presence of Pyridine at 0°.

The reaction was carried out by the general procedure discussed above. Work-up of the reaction mixture was accomplished by the method described for the addition of iodonium nitrate to the same olefin.

Reaction of 4-Bromo-2,3-dimethylbut-2-en-1-yl Nitrate, **245** with Pyridine in Chloroform.

A mixture of 0.224 g (1 mmol) of 4-bromo-2,3-dimethylbut-2-en-1-yl nitrate, 2 ml of pyridine and 10 ml of chloroform was allowed to stand overnight. Ether was added to the reaction mixture and the resulting precipitate collected. Recrystallization from methanol-ether gave the dipyridinium salt, **241** in almost quantitative yield.

Reaction of 5-Bromohex-3-en-2-yl Nitrate, **246** with Pyridine in Chloroform.

The reaction was carried out by the procedure described above for **245**. Thus reaction of 0.224 g (1 mmol) of 5-bromo-hex-3-en-2-yl nitrate with 2 ml of pyridine in 10 ml of chloroform gave the dipyridinium salt, **244** as an oil in almost quantitative yield.

Procedure for the Reaction of Bromonium Nitrate with Phenylacetylene.

The procedure was the same as that used for the reaction of iodonium nitrate with terminal alkynes. β-Bromophenylacetylene was obtained in 63% yield. b.p. 30.5°/0.07 mm. (lit., 84-85°/10 mm)[193].

Procedure for the Reaction of Bromonium Nitrate with Pent-4-en-1-ol in Chloroform-Pyridine.

The reaction was performed by the general procedure describe above. Separation of the cyclic ether and hydroxy-bromonitrate esters was accomplished by chromatography on florisil and elution with petroleum ether-chloroform (9:1) and then with chloroform-methanol (9:1). Evaporation of the first fraction gave 0.65 g (20%) of 2-bromomethyltetrahydrofuran, 267.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 1.65-2.3 (m, 4H, 2 $-CH_2-$); 3.4 (t, 2H, $-CH_2Br$, J=5 Hz, 6.5 Hz); 3.5-4.3 (m, 2H, $-CH_2-O$, $-CH-O$).

Evaporation of the second fraction gave a mixture of hydroxy-bromonitrate esters, 265 and 266. Yield 29%.

From the ether insoluble residue was isolated by the usual procedure a mixture of bromopyridinium salts, 268 and 269. Yield 20%.

3,3,3-Triphenylpropene.

This compound was prepared according to Scheme 10, by reported procedures. m.p. 80-81° (lit., m.p. 80-81°).

Reaction of Bromonium Nitrate with 3,3,3-Triphenylpropene in Chloroform-Pyridine.

The reaction was carried out by the general procedure described above. No bromonitrate ester was isolated. Crystallization of the ether insoluble residue from ethanol-ether gave a mixture of compound, 272 and pyridinium bromide (yield 3.75 g). Purification was effected as follows:

A mixture of 1 g of the crude reaction product, 1 g of potassium carbonate and 25 ml of water was heated on a steam bath to about 50° whereupon dissolution occurred. On cooling a solid separated, which was collected. Recrystallization from methanol-ether gave 0.6 g of pure N-[1-(2,3,3-triphenyl)prop-2-enyl]pyridinium nitrate, 272, m.p. 211-212°.

Anal. Calcd. for $C_{26}H_{22}N_2O_3$: C, 76.1; H, 5.37; N, 6.83. Found: C, 75.71; H, 5.40; N, 6.75.

The n.m.r. spectrum: $\delta_{TMS}[(CD_3)_2SO]$: 5.72 (s, 2H, $-CH_2-$); 7-7.64 (m, 15H, 3Ph); 7.9-9.17 (m, 5H, pyridine hydrogens).

The melting point and n.m.r. spectrum were identical to those of an authentic sample synthesized as follows:

Synthesis of N-[1-(2,3,3-Triphenyl)prop-2-enyl]pyridinium Nitrate, 272.

To a solution of 0.64 g (2.37 mmol) of 3,3,3-triphenylpropene in 15 ml of carbon tetrachloride was added a solution of 0.3972 g (2.37 mmol) of bromine in 5 ml of carbon tetrachloride and the mixture allowed to stand for 48 h. The solvent was removed *in vacuo* and the residual solid taken up in 20 ml of carbon tetrachloride. To the solution 1 ml of pyridine was added and the mixture allowed to stand for 3 h. The precipitated solid was collected and taken up in 50 ml of hot water. Addition of a few drops of concentrated nitric acid and cooling gave a precipitate, which was collected. Recrystallization from methanol-ether gave 0.7 g (72%) of N-[1-(2,3,3-triphenyl)prop-2-enyl]pyridinium nitrate, 272.

Addition of Bromonium Nitrate to (Z)-β-Deuterostyrene in Chloroform-Pyridine.

The reaction was carried out by the general procedure discussed before. Thus reaction of 3.78 g (0.036 mol) of (Z)-β-deuterostyrene with bromonium nitrate (0.04 mol) in 60 ml of chloroform and 25 ml of pyridine at 0° for 3 h and work-up by the usual procedure gave 4.5 g (46%) of threo-2-deutero-2-bromo-1-phenylethyl nitrate, **288**.

The n.m.r. spectrum: δ_{TMS} ($CDCl_3$): 3.62 (d, further split by H-D-coupling, 1H, -CHD-Br, $J_{\underline{CH}-\underline{CH}D}=7.5$ Hz); 6.0 (d, 1H, -CH-ONO$_2$, $J_{\underline{CH}-\underline{CH}-D}=7.5$ Hz); 7.37 (m, 5H, Ph).

The i.r. spectrum: ν_{max} (liquid film): 1630, 1275 cm^{-1} (-ONO$_2$).

From the ether insoluble residue and by the procedure described for the addition of iodonium nitrate to (Z)-β-deuterostyrene was isolated 2.5 g (26.5%) of (Z)-N-[1-(2-deutero-1-phenyl)ethenyl]-pyridinium bromide, **289**.

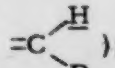
The n.m.r. spectrum: δ_{TMS} [$(CD_3)_2SO$]: 6.43 (s, 1H,  $=C\genfrac{}{}{0pt}{}{\diagup H}{\diagdown D}$); 7.45 (m, 5H, Ph); 8.17-9.27 (m, 5H, pyridine hydrogens).

Table 19. Iodo-nitrate Esters.

Alkene	Iodo-nitrate Ester	Boiling Point (°C/mm)	Yield (%)	Formula	Observed %			Calculated %			Molecular Ion
					C	H	N	C	H	N	
Hex-1-ene	1-Iodohex-2-yl nitrate	80/0.5	41	$C_6H_{12}NO_3I$	26.35	4.79	4.73	26.39	4.42	5.12	-
3,3-Dimethylbut-1-ene	2-Iodo-3,3-dimethylbut-1-yl nitrate	55/0.2	26	$C_6H_{12}NO_3I$	26.37	4.80	4.70	26.39	4.42	5.12	M-ONO_2 211
3,4-Dimethylhex-1-ene	1-Iodo-3,4-dimethylhex-2-yl nitrate 2-Iodo-3,4-dimethylhex-1-yl nitrate	93-97/0.5*	75	$C_8H_{16}NO_3I$	32.30	5.60	4.37	31.90	5.35	4.65	301
Cyclopentene	2-Iodocyclopentyl nitrate	40/0.5	54	$C_5H_8NO_3I$	23.48	3.19	5.42	23.35	3.11	5.45	M-I 130
Cyclohexene	2-Iodocyclohexyl nitrate	113/1.3	60	$C_6H_{10}NO_3I$	26.84	3.87	4.98	26.58	3.72	5.16	271
Cycloheptene	2-Iodocycloheptyl nitrate	85/0.05	68	$C_7H_{12}NO_3I$	29.93	4.52	4.84	29.50	4.21	4.91	285
Cyclooctene	2-Iodocyclooctyl nitrate	97/0.02	79	$C_8H_{14}NO_3I$	32.71	5.08	4.37	33.62	4.90	4.90	299
Norbornene†	2-Iodonorborn-3-yl nitrate	83/0.3	60	$C_7H_{10}NO_3I$	30.55	3.50	4.33	29.70	3.56	4.95	M-I 156
1,5-Hexadiene	6-Iodohex-1-en-5-yl nitrate	62/0.35	85	$C_6H_{10}NO_3I$	26.51	3.34	4.89	26.59	3.72	5.16	271
Norbornadiene	Tricyclo[2.2.1.0^{2,6}]-5-iodohept--3-yl nitrate	75/0.08	64	$C_7H_8NO_3I$	30.05	3.18	5.05	29.92	2.87	4.93	M-ONO_2 219
1,4-Cyclohexadiene	5-Iodocyclohexen-4-yl nitrate	50/0.5	27	$C_6H_8NO_3I$	26.91	3.23	5.22	26.79	3.00	5.20	M-I 142
4-Vinylcyclohex-1-ene	2(1)-Iodo-4-vinylcyclohexyl nitrate	89/0.4	25	$C_8H_{12}NO_3I$	32.91	4.05	4.20	32.83	3.96	4.71	M-I 170
Styrene	2-Iodo-1-phenylethyl nitrate	110/1	10		-	-	-	-	-	-	293

* Isomeric mixture.

† Nortricyclanyl iodide was produced in 40% yield, b.p. 40°/0.15 mm. Molecular ion 220. See text.

Table 20. Iodopyridinium Salts.

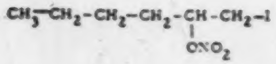
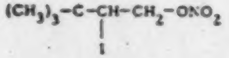
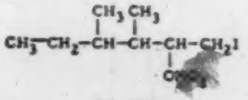
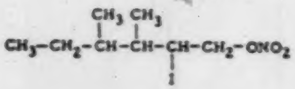
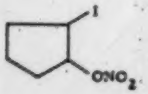
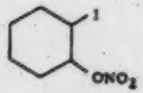
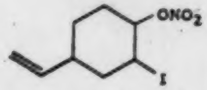
Alkene	Iodopyridinium Salt	Melting Point (°C)	Yield (%)	Formula	Observed %			Calculated %		
					C	H	N	C	H	N
Hex-1-ene	N-[2-(1-Iodohexyl)]pyridinium nitrate	Oil	42	-	-	-	-	-	-	-
3,3-Dimethylbut-1-ene	N-[1-(2-Iodo-3,3-dimethylbutyl)]-pyridinium nitrate	133	49	$C_{11}H_{17}N_2O_3I$	36.10	4.70	7.60	35.90	4.65	7.60
Cyclopentene	N-(2-Iodocyclopentyl)pyridnium nitrate	Oil	9	$C_{10}H_{13}N_2O_3I$	34.13	3.96	8.94	35.73	3.89	8.33
Cyclohexene	N-(2-Iodocyclohexyl)pyridinium nitrate	145-150	40	$C_{11}H_{15}N_2O_3I$	37.77	4.80	7.97	37.73	4.32	8.00
Cycloheptene	N-(2-Iodocycloheptyl)pyridinium nitrate	140-142	11	$C_{12}H_{17}N_2O_3I$	39.82	4.87	-	39.60	4.67	-
Cyclooctene	N-(2-Iodocyclooctyl)pyridinium nitrate	152-153	5.5	$C_{13}H_{19}N_2O_3I$	41.36	4.99	7.36	41.27	5.03	7.41
1-Methylcyclohexene	N-[1-(1-Methyl-2-iodocyclohexyl)]-pyridinium nitrate	70	25	$C_{12}H_{17}N_2O_3I$	39.24	4.71	8.27	39.57	4.70	7.69
2,3-Dimethylbut-2-ene	N-[2-(2,3-Dimethyl-3-iodobutyl)]-pyridinium nitrate	105 (dec)	47	$C_{11}H_{17}N_2O_3I$	37.79	4.50	7.85	37.51	4.86	7.95
2-Methylbut-2-ene	N-[2-(2-Methyl-3-iodobutyl)]pyridinium nitrate	121-123	80	$C_{10}H_{15}N_2O_3I$	35.38	4.63	8.01	35.50	4.47	8.28
Norbornadiene	N-[3-(5-Iodonortricyclanyl)]pyridinium nitrate	118-125 (dec)	10	$C_{12}H_{13}N_2O_3I$	40.31	3.80	8.20	40.02	3.64	7.78
1,4-Cyclohexadiene	N-[4-(5-Iodocyclohexenyl)]pyridinium nitrate	156-157 (dec)	24	$C_{11}H_{13}N_2O_3I$	37.80	3.96	7.90	37.95	3.76	8.04
4-Vinylcyclohex-1-ene	N-[1(2)-2(1)-Iodo-4-vinylcyclohexyl)]-pyridinium nitrate	93-98	26.5	$C_{13}H_{17}N_2O_3I$	41.75	4.70	-	41.50	4.55	-
2,4-Hexadiene	N-[4-(5-Iodo-2-hexenyl)]pyridinium nitrate	116-117 (dec)	70	$C_{11}H_{15}N_2O_3I$	37.77	4.34	8.13	37.73	4.32	8.00
1,3-Cyclohexadiene	N-[3-(4-Iodocyclohexenyl)]pyridinium nitrate	118	60	$C_{11}H_{13}N_2O_3I$	38.20	3.74	7.80	37.95	3.76	8.04

Continued . . .

Table 20 - Continued

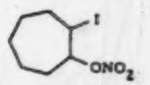
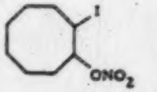
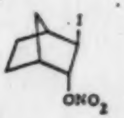
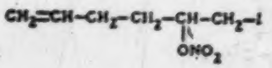
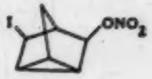
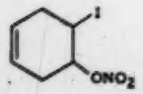
Alkene	Iodopyridinium Salt	Melting Point (°C)	Yield (%)	Formula	Observed %			Calculated %		
					C	H	N	C	H	N
Ethyl vinyl ether	N-[1-(1-Ethoxy-2-iodoethyl)]-pyridinium nitrate	66-69	75	$C_9H_{13}N_2O_4I$	31.70	3.70	8.50	31.78	3.85	8.23
Dihydropyran	N-(3-Iodotetrahydropyranosyl)-pyridinium nitrate	113-116	72	$C_{10}H_{13}N_2O_4I$	33.80	3.70	7.81	34.10	3.72	7.95
Styrene	N-[1-(1-Phenylethenyl)]pyridinium iodide	155	40	$C_{13}H_{12}NI$	50.90	4.00	-	50.50	3.91	-
p-Methoxychalcone	N-[1-(2-Iodo-2-benzoyl-1-para-methoxyphenylethyl)]pyridinium nitrate	178-179 (dec)	91	$C_{21}H_{19}N_2O_5I$	49.73	3.72	5.57	49.79	3.75	5.53

Table 21. Spectroscopic Properties of Iodo-nitrate Esters.ᵃ

Compound	$\delta_{TMS}^{CDCl_3}$ -CH-I	-CH-ONO$_2$	-CH$_2$-I	-CH$_2$-ONO$_2$	Additional Absorptions
 $CH_3-CH_2-CH_2-CH_2-\underset{\underset{\displaystyle ONO_2}{\vert}}{CH}-CH_2-I$	-	4.9 (1H) m	3.35 (2H) d J=5.5 Hz	-	1.3 (m, 9H, 3 $-CH_2-$, $-CH_3$)
 $(CH_3)_3-C-\underset{\underset{\displaystyle I}{\vert}}{CH}-CH_2-ONO_2$	4.17 (1H) m	-	-	4.8 (2H) m	1.15 (s, 9H, $-C(CH_3)_3$)
 $CH_3-CH_2-\overset{\overset{\displaystyle CH_3}{\vert}}{CH}-\overset{\overset{\displaystyle CH_3}{\vert}}{CH}-\underset{\underset{\displaystyle ONO_2}{\vert}}{CH}-CH_2I$  $CH_3-CH_2-\overset{\overset{\displaystyle CH_3}{\vert}}{CH}-\overset{\overset{\displaystyle CH_3}{\vert}}{CH}-\underset{\underset{\displaystyle I}{\vert}}{CH}-CH_2-ONO_2$	4.8 (1H) m	5.0	3.4 (1.4H) m	4.4 (0.6H) m	0.8-2 (m, 13H, 2 $-CH-$, $-CH_2-$, 3 $-CH_3$)
	4.2 (1H) m	5.4 (1H) m	-	-	2.0 (m, 6H, 3 $-CH_2-$)
	4.17 (1H) m	5.15 (1H) m	-	-	1.7 (m, 8H, 4 $-CH_2-$)
	4.5 (1H) m	4.9 (1H) m	-	-	2.0 (m, 7H, $-CH-$, 3 $-CH_2$) 5.15, 5.7 (m, 3H, $-CH=CH_2$)

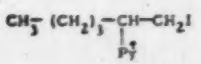
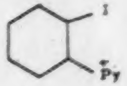
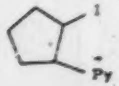
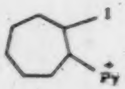
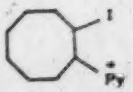
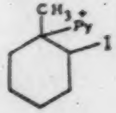
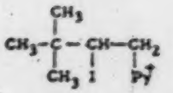
Continued . . .

Table 21 - Continued

Compound	$\delta_{TMS}^{CDCl_3}$				
	$-CH-I$	$-CH-ONO_2$	$-CH_2-I$	$-CH_2-ONO_2$	Additional Absorptions
	4.35 (1H) m	5.36 (1H) m	-	-	1.5-2.4 (m, 10H, 5 $-CH_2$)
	4.3 (1H) m	5.4 (1H) m	-	-	1.1-2.3 (m, 12H, 6 $-CH_2-$)
	3.75 (1H) m	5.5 (1H) m	-	-	1.3-2.8 (m, 8H, 2 $-CH-$, 3 $-CH_2-$)
 $CH_2{=}CH-CH_2-CH_2-\underset{ONO_2}{\underset{\mid}{C}H}-CH_2-I$	-	4.9 (1H) m	3.35 (2H) d J=5.5 Hz	-	2.0 (m, 4H, 2 $-CH_2-$) 5.15, 5.6 (m, 3H, $-CH{=}CH_2$)
	4.25 (1H) m	5.03 (1H) m	-	-	1.75, 2.5 (m, 6H, 4 $-CH-$, $-CH_2-$)
	4.38 (1H) m	5.27 (1H) m	-	-	2.7 (m, 4H, 2 $-CH_2-$) 5.6 (m, 2H, $-CH{=}CH-$)

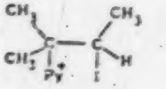
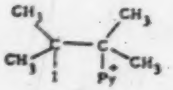
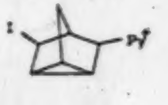
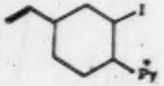
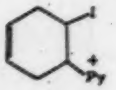
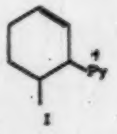
* All these compounds had $-ONO_2$ absorption in the i.r. spectrum between 1620 and 1640 cm^{-1}.

Table 22. Spectroscopic Properties of Iodoalkyl Pyridinium Nitrates.*

Compounds†	$\delta_{TMS}^{(CD_3)_2SO}$ -CH-I	$-CH-\overset{+}{N}<$	$-CH_2-I$	$-CH_2-\overset{+}{N}<$	Other hydrogens
 $CH_3-(CH_2)_3-\underset{\overset{+}{Py}}{CH}-CH_2I$	-	5.2 (1H) m	4.05 (2H) m	-	0.6-2.5 (m, 9H, 3 $-CH_2$, $-CH_3$)
	4.9 (2H) m		-	-	2.1 (m, 8H, 4 $-CH_2-$)
	4.6 (1H) m	5.2 (1H) m	-	-	2.1 (m, 6H, 3 $-CH_2-$)
	5.0 (2H) m		-	-	1.7, 2.25 (m, 10H, 5 $-CH_2-$)
	4.8-5.5 (2H) m		-	-	1.7, 2.3 (m, 12H, 6 $-CH_2-$)
	4.85 (1H) m	-	-	-	2.05 (s, 3H, $-CH_3$); 1.7, 2.3 (m, 8H, 4 $-CH_2-$)
 $CH_3-\overset{CH_3}{\underset{CH_3}{C}}-\underset{I}{CH}-\underset{\overset{+}{Py}}{CH_2}$	5.1 (1H) m	-	-	4.9 (2H) m	1.2 (s, 9H, $-C(CH_3)_3$)

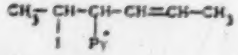
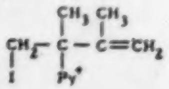
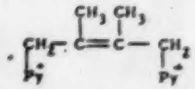
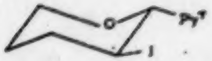
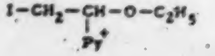
Continued . . .

Table 22 - Continued

Compounds*	δ_{TMS} $(CD_3)_2SO$ $-CH-I$	$-CH-\overset{+}{N}<$	$-CH_2-I$	$-CH_2-\overset{+}{N}<$	Other hydrogens
	5.1 (1H) q J=7 Hz	-	-	-	1.9 (d, 3H, $CH_3-\overset{|}{\underset{|}{C}}-I$, J=7 Hz); 1.97 (s, 6H, $(CH_3)_2-\overset{|}{C}-\overset{+}{N}<$).
	-	-	-	-	2.08 (s, 6H, $(CH_3)_2-\overset{|}{C}-I$); 2.05 (s, 6H, $(CH_3)_2-\overset{|}{C}-\overset{+}{N}<$).
	4.3 (0.56H) s 3.8 (0.44H) s	5.0 (1H) s *	-	-	2.75 (s, 1H); 1.95 (m, 4H); 1.1 (m, 1H).
	4.9 (1H) m	5.1 (1H) m	-	-	2.2 (m, 6H, 3 $-CH_2-$), 2.85 (m, 1H, $-CH-C=C$); 6.3, 5.35 (m, 3H, olefinic hydrogens).
	5.0 (1H) m	5.2 (1H) m	-	-	2.9 (m, 4H, 2 $-CH_2-$), 5.65 (m, 2H, olefinic hydrogens).
	4.85 (1H) m	$5.6^{\ddagger}$ (2H) m	-	-	2.35 (m, 4H, 2 $-CH_2-$); 6.3 (m, 1H, one olefinic hydrogen).

Continued . . .

Table 22 - Concluded

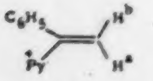
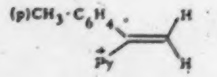
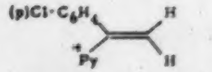
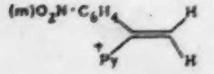
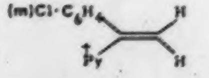
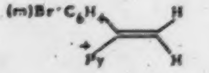
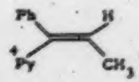
Compounds†	δ_{TMS} $(CD_3)_2SO$				
	$-CH-I$	$-CH-\overset{+}{N}<$	$-CH_2-I$	$-CH_2-\overset{+}{N}<$	Other hydrogens
 $CH_3-\underset{I}{CH}-\underset{\overset{+}{Py}}{CH}-CH=CH-CH_3$	4.9 (1H) m	5.75 (1H) m			1.75 (d, 3H, $CH_3-C=C$, J=5 Hz); 2.0 (d, 3H, CH_3-C-I, J=7 Hz); 6.1, 5.85 (m, 2H, olefinic hydrogens).
 $\underset{I}{CH_2}-\overset{CH_3}{\underset{\overset{+}{Py}}{C}}-\overset{CH_3}{C}=CH_2$	4.3 (2H) s				1.67 (s., 3H, $CH_3-C=C$); 2.03 (s, 3H, $CH_3-C-\overset{+}{N}<$); 5.28 (s, 1H, one olefinic hydrogen), 5.41 (m, 1H, one olefinic hydrogen).
 $\underset{\overset{+}{Py}}{CH_2}-\overset{CH_3}{C}=\overset{CH_3}{C}-\underset{\overset{+}{Py}}{CH_2}$				5.4 (4H) s	1.82 (s, 6H, 2 $-CH_3$).
	4.8 (1H) *	6.38 (1H) d J=10 Hz			2.2 (m, 3H), 4.2 (m, 3H).
 $I-CH_2-\underset{\overset{+}{Py}}{CH}-O-C_2H_5$		6.23 (1H) t J=5 Hz	3.82 (2H) d J=5 Hz		1.2 (t, 3H, $-CH_3$, J=6 Hz), 3.62 (m, 2H, $-CH_2-$).

† Unless otherwise indicated the counter ion was nitrate.

* All these compounds had absorption due to $\overset{+}{Py}$ between δ 8-9.5.

‡ Includes one of the olefinic protons.

Table 23. Spectroscopic Properties of N- 1-(1-arylethenyl) pyridinium iodides*.

Compounds	$\delta_{TMS}^{(CD_3)_2SO}$				
	H^a	H^b	$-J_{a,b}$ (Hz)	Aromatic hydrogens	Additional absorptions
 C_6H_5 H^b $\overset{+}{Py}$ H^a	6.1 (d)	6.45 (d)	2.6	7.4 (m, 5H)	-
 (p)CH_3·C_6H_4 H $\overset{+}{Py}$ H	6.0 (d)	6.4 (d)	2.7	7-7.6 (m, 4H)	2.36 (s, 3H, CH_3)
 (p)Cl·C_6H_4 H $\overset{+}{Py}$ H	6.48 (d)	6.83 (d)	3.0	7.5-8.2 (m, 4H)	-
 (m)O_2N·C_6H_4 H $\overset{+}{Py}$ H	6.3 (d)	6.7 (d)	3.0	7.7-8.3 (m, 4H)	-
 (m)Cl·C_6H_4 H $\overset{+}{Py}$ H	6.15 (d)	6.56 (d)	3.0	7.2-7.8 (m, 4H)	-
 (m)Br·C_6H_4 H $\overset{+}{Py}$ H	6.13 (d)	6.53 (d)	2.8	7.3-7.9 (m, 4H)	-
 Ph H $\overset{+}{Py}$ CH_3	-	6.6 (q) J=7 Hz	-	7.45 (m, 5H)	1.95 (q, 3H, CH_3, J=7 Hz)

* All these compounds had absorptions due to $\overset{+}{Py}$ between δ 8-9.5.

Table 24. Iodo-phenols and Iodo-anilines.

Substrate	Product	Melting point (°C)		Yield	Formula	Molecular weight	
		Observed	Literature	(%)		Observed	Calculated
2-Allylphenol	4,6-Di-iodo-2-allylphenol	Oil		74.5	$C_9H_8OI_2$	385.8688	385.8664
Phenol	2,4,6-Tri-iodophenol	160	158-159[194]	94	-	-	-
4-Methylphenol	2,6-Di-iodo-4-methylphenol	61	62[195]	90	$C_7H_6OI_2$	359.8501	359.8508
Aniline	2,4-Di-iodoaniline	95	95-96[196]	46	$C_6H_5NI_2$	344.8525	344.8512
4-Methylaniline	2,6-Di-iodo-4-methylaniline	123	125[197]	23	$C_7H_7NI_2$	358.8658	358.8668
N-Methylaniline	2,4-Di-iodo-N-methylaniline	Oil	-	78	$C_7H_7NI_2$	358.8662	358.8668
N,N-Dimethylaniline	4-Iodo-N,N-dimethylaniline	83	82[198]	95	$C_8H_{10}NI$	246.9845	246.9858

Table 25. Spectroscopic Properties of Iodo-phenols and Iodo-anilines.

Compound	I.r. $_{max}$ cm^{-1}	N.m.r. δ_{TMS} CDCl$_3$
4,6-Di-iodo-2-allylphenol	3845 (-OH), 1633 (-C C-) 1442 (C-O-)	7.8 (d, 1H, H^3, $J_{3,5}$=2 Hz); 7.4 (d, 1H, H^5, $J_{5,3}$=2 Hz); 5.5-6.3 (m, 1H, -CH=CH$_2$); 5.4 (s, 1H, -OH); 4.8-5.3 (m, 2H, -CH$_2$); 3.4 (d, 2H, -CH$_2$-).
2,4,6-Tri-iodophenol	3475 (OH)	7.9 (s, 2H, H^3, H^5); 5.75 (s, 1H, -OH).
2,6-Di-iodo-4-methylphenol	3480 (-OH)	7.45 (s, 2H, H^3, H^5); 5.5 (s, 1H, -OH); 2.2(s, 3H, -CH$_3$).
2,4-Di-iodoaniline	3475, 3380 (-NH$_2$)	7.87 (d, 1H, H^3, $J_{3,5}$=2 Hz); 7.35 (q, 1H, H^5, $J_{5,3}$=2 Hz, $J_{5,6}$=8.5 Hz); 6.43 (d, 1H, H^6, $J_{5,6}$=8.5 Hz); 6.1 (broad singlet, 2H, -NH$_2$).
2,6-Di-iodo-4-methylaniline	3460, 3370 (-NH$_2$)	7.4 (s, 2H, H^3, H^5); 4.4 (broad singlet, 2H, -NH$_2$); 2.15 (s, 3H, -CH$_3$).
2,4-Di-iodo-N-methylaniline	3405 (-NH-)	7.85 (d, 1H, H^3, $J_{3,5}$=2 Hz); 7.4 (q, 1H, H^5, $J_{5,3}$=2 Hz, $J_{5,6}$=8.5 Hz); 6.27 (d, 1H, H^6, $J_{5,6}$=8.5 Hz); 6.2 broad singlet, 1H, -NH-); 2.83 (s, 3H, -CH$_3$).
4-Iodo-N,N-dimethylaniline		7.45 (d, 2H, H^3, H^5, $J_{2,3}$=$J_{5,6}$=9 Hz); 6.47 (d, 2H) 2.9 (s, 6H, 2 -CH$_3$).

Table 26. Yields (%) of Iodo-nitrate Esters, Iodo-pyridinium Salts and Cyclic Ethers from the Reaction of Iodonium Nitrate with Olefinic Alcohols.

Olefinic Alcohol	In Pyridine			In *sym*-Collidine	
	Iodo-nitrate ester	Iodo-pyridinium salt	Cyclic ether	Iodo-nitrate ester	Cyclic ether
Allyl alcohol	30[a]	23[2]	0	60[a]	0
2-Methylallyl alcohol	0	75	0	-	-
1,1-Dimethylallylalcohol	20	40	5	20	20
Hex-1-en-3-ol	34[a]	16	0	53[a]	11
But-3-en-1-ol	34[a]	54[a]	0	-	-
3-Methylbut-3-en-1-ol	0	61	0	-	-
Z-Hex-3-en-1-ol	62[a]	10	0	59[a]	0
Hex-5-en-3-ol	10[a]	0	20[b]	17[a]	30
1-Allylcyclohexanol	55	15	10	60	0
2-Allylphenol	13	0	33.5	-	-
2-Allyl-6-methylphenol	15	0	33.5	-	-
Pent-4-en-1-ol	6[a]	0	60	-	-
Hex-5-en-1-ol	21[a]	39	17	-	-
Anti-7-Norbornenol	74	0	0	-	-
Endo-*cis*-5-Norbornene-2,3-dimethanol	0	0	74	-	-
Trans-5-Norbornene-2,3-dimethanol	0	0	86	-	-
Exo-*cis*-5-Norbornene-2,3-dimethanol	40	0	?	-	-
Cyclohex-2-en-1-ol	36	29	0	44	0
Cyclopent-2-en-1-ol	52	22	0	-	-
Cyclohept-2-en-1-ol	59[a]	35	0	-	-
Cyclooct-2-en-1-ol	60	0	0	-	-

[a] Mixture of isomers.

[b] N-(5-Ethyltetrahydrofuran-3-yl)pyridinium nitrate.

Table 27. Hydroxy-iodoalkyl Nitrates and Cyclic Ethers.

Unsaturated alcohol	Product	Boiling point (°C/mm)	Formula	Observed %			Calculated %		
				C	H	N	C	H	N
Allyl alcohol	3-Hydroxy-1-iodoprop-2-yl nitrate 3-Hydroxy-2-iodoprop-2-yl nitrate	78/0.15	$C_3H_6NO_4I$	-	-	5.9	-	-	5.7
1,1-Dimethylallyl alcohol	3-Hydroxy-2-iodo-3-methylbut-1-yl nitrate	70/0.1	$C_5H_{10}NO_4I$	22.1	3.7	4.55	21.8	3.65	5.00
Hex-1-en-3-ol	3-Hydroxy-1-iodohex-2-yl nitrate 3-Hydroxy-2-iodohex-1-yl nitrate	90/0.1	$C_6H_{12}NO_4I$	24.95	4.2	4.7	24.95	4.2	4.85
Hex-5-en-3-ol	4-Hydroxy-1-iodohex-2-yl nitrate 4-Hydroxy-2-iodohex-1-yl nitrate	65/0.1	$C_6H_{12}NO_4I$	-	-	5.0	-	-	4.85
1-Allylcyclohexanol	4-Hydroxy-4,4-pentamethylene-1-iodobut-2-yl nitrate	-	$C_9H_{16}NO_4I$	*[M-Found 329.0113]			[M-Calc. 329.0124]		
2-Allylphenol	3-(2-Hydroxy-3,5-di-iodo)phenyl-1-iodoprop-2-yl nitrate	-	$C_9H_8NO_4I_3$	*[M-Found 574.7598]			[M-Calc. 574.7587]		
2-Allyl-6-methylphenol	3-(2-Hydroxy-5-iodo-3-methyl)phenyl-1-iodoprop-2-yl nitrate	-	$C_{10}H_{11}NO_4I_2$	*[M-Found 462.8773]			[M-Calc. 462.8776]		
Cyclohex-2-en-1-ol	3-Hydroxy-2-iodocyclohexyl nitrate	90/0.05	$C_6H_{10}NO_4I$	25.3	3.4	4.2	25.1	3.5	4.9
Cyclopent-2-en-1-ol	3-Hydroxy-2-iodocyclopentyl nitrate	46-47†	$C_5H_8NO_4I$	21.97	2.98	5.04	21.98	2.93	5.13
Cyclohept-2-en-1-ol	3-Hydroxy-2-iodocycloheptyl nitrate	-	$C_7H_{12}NO_4I$	*[M-Found 300.9811]			[M-Calc. 300.9811]		
1,1-Dimethylallyl alcohol	2,3-Epoxy-1-iodo-3-methylbutane	52/6	C_5H_9OI	28.5	4.2	-	28.3	4.3	-
Hex-1-en-3-ol	3-Iodo-2-propyl oxetan	72/2	$C_6H_{11}OI$	31.75	4.75	-	31.9	2.9	-
Hex-5-en-3-ol	5-Ethyltetrahydrofuran-3-yl nitrate	60/1	$C_6H_{11}NO_4$			8.1			8.7
2-Allylphenol	2-Iodomethyl-5,7-di-iodobenzo[b]-2,3-dihydrofuran	-	$C_9H_7OI_3$	*[M-Found 511.7631]			[M-Calc. 511.7631]		
2-Allyl-6-methylphenol	2-Iodomethyl-5-iodo-6-methylbenzo[b]-2,3-dihydrofuran	-	$C_{10}H_{10}OI_2$	*[M-Found 399.8828]			[M-Calc. 399.8822]		

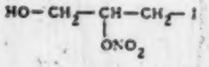
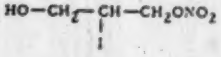
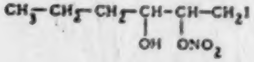
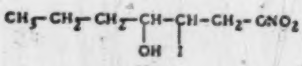
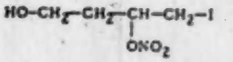
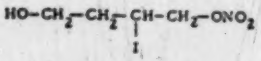
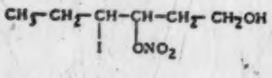
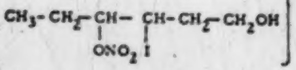
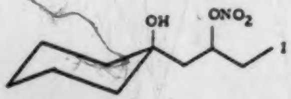
* Determined by mass spectrometry.

† Melting point (ether-hexane).

Table 28. Hydroxy-iodoalkyl Pyridinium Salts.

Unsaturated alcohol	Pyridinium salt	Melting point (°C)	Formula	Observed %			Calculated %		
				C	H	N	C	H	N
Allyl alcohol	N-[2-(3-Hydroxy-1-iodopropyl)]pyridinium nitrate								
	N-[1-(3-Hydroxy-2-iodopropyl)]pyridinium nitrate	48-52	$C_8H_{11}N_2O_4I$	30.2	3.18	8.8	29.45	3.4	8.6
2-Methylallyl alcohol	N-[2-(3-Hydroxy-1-iodo-2-methylpropyl)]-pyridinium nitrate	108-110	$C_9H_{13}N_2O_4I$	32.2	4.0	8.5	31.8	3.85	8.25
1,1-Dimethylallyl alcohol	N-[1-(3-Hydroxy-2-iodo-3,3-dimethylpropyl)]-pyridinium nitrate	123	$C_{10}H_{15}N_2O_4I$	34.3	4.2	7.65	33.9	4.25	7.91
Hex-1-en-3-ol	N-[1-(3-Hydroxy-2-iodohexyl)] pyridinium nitrate	80-85	$C_{11}H_{17}N_2O_4I$	36.15	4.7	7.2	35.9	4.65	7.61
3-Methylbut-3-en-1-ol	N-[2-(4-Hydroxy-1-iodo-2-methylbutyl)]-pyridinium nitrate	107-108	$C_{10}H_{15}N_2O_4I$	33.94	4.56	7.52	33.9	4.25	7.91
Z-Hex-3-en-1-ol	N-[3(4)-6-Hydroxy-4(3)-iodohexyl]-pyridinium nitrate	130-131	$C_{11}H_{17}N_2O_4I$	35.9	4.59	7.31	35.9	4.65	7.61
Hex-5-en-3-ol	N-[3-(5-Ethyltetrahydrofuranyl)] pyridinium nitrate	Oil	$C_{11}H_{16}N_2O_4 \cdot H_2O$	50.85	6.5	10.6	51.1	7.0	10.8
Cyclohex-2-en-1-ol	N-[1-(3-Hydroxy-2-iodocyclohexyl)]-pyridinium nitrate	166-168	$C_{11}H_{15}N_2O_4I$	36.1	4.0	8.0	36.1	4.1	7.65
Cyclopent-2-en-1-ol	N-[1-(3-Hydroxy-2-iodocyclopentyl)]-pyridinium nitrate	137-139	$C_{10}H_{13}N_2O_4I$	34.14	3.68	7.91	34.1	3.69	7.96
Cyclohept-2-en-1-ol	N-[1-(3-Hydroxy-2-iodocycloheptyl)]-pyridinium nitrate	148	$C_{12}H_{17}N_2O_4I$	37.92	4.69	7.22	37.9	4.47	7.37

Table 29. Spectroscopic Properties of Hydroxy-iodoalkyl Nitrates* and Cyclic Ethers.

Compounds	$\delta_{TMS}^{CDCl_3}$				
	$-CH-I$	$-CH-ONO_2$	$-CH_2-I$	$-CH_2-ONO_2$	Additional absorptions
 $\mathrm{HO-CH_2-\underset{ONO_2}{\underset{\vert}{CH}}-CH_2-I}$	-	5.15 (0.8H) m	3.42 (1.6H) d J=6 Hz	-	3.3 (s, 1H, $-OH$)
 $\mathrm{HO-CH_2-\underset{I}{\underset{\vert}{CH}}-CH_2ONO_2}$	4.35 (0.2 H) m	-	-	4.83 (0.4H) t J=6 Hz, 7 Hz	3.95 (m, 2H, $-\underline{CH_2}OH$)
 $\mathrm{CH_3-CH_2-CH_2-\underset{OH}{\underset{\vert}{CH}}-\underset{ONO_2}{\underset{\vert}{CH}}-CH_2I}$	-	4.95 (0.5H) m	3.47 (1H) d J=6 Hz	-	0.97 (m, 3H, $-CH_3$) 1.5 (m, 4H, 2 $-CH_2-$)
 $\mathrm{CH_3-CH_2-CH_2-\underset{OH}{\underset{\vert}{CH}}-\underset{I}{\underset{\vert}{CH}}-CH_2-ONO_2}$	4.4 (0.5 H) m	-	-	4.87 (1H) d J=7.5 Hz	2.43 (s, 1H, OH) 3.0, 3.9 (m, 1H, $-\underline{CH}-OH$)
 $\mathrm{HO-CH_2-CH_2-\underset{ONO_2}{\underset{\vert}{CH}}-CH_2-I}$	-	5.17 (0.85H) m	3.43 (1.7H) d J=5 Hz	-	1.85-2.2 (m, 3H, $-CH_2-$, $-OH$) 3.78 (t, 2H, $-\underline{CH_2}-OH$, J=6 Hz)
 $\mathrm{HO-CH_2-CH_2-\underset{I}{\underset{\vert}{CH}}-CH_2-ONO_2}$	4.3 (0.15H) m	-	-	4.75 (0.3H) t J=4 Hz, 6.5 Hz	
Threo  $\mathrm{CH_3-CH_2-\underset{I}{\underset{\vert}{CH}}-\underset{ONO_2}{\underset{\vert}{CH}}-CH_2-CH_2OH}$	4.1-5.6 (2H) 4m	-	-	-	1.1 (m, 3H, $-CH_3$) 1.7-2.3 (m, 4H, 2 $-CH_2-$)
Threo  $\mathrm{CH_3-CH_2-\underset{ONO_2}{\underset{\vert}{CH}}-\underset{I}{\underset{\vert}{CH}}-CH_2-CH_2OH}$					3.45 (s, 1H, $-OH$) 3.9 (m, 2H, $-\underline{CH_2}OH$)
		5.23 (1H) quint J=5.5 Hz	3.4 (2H) d J=5.5 Hz	-	1.5 (m, 10H, 5 $-CH_2-$) 1.9 (m, 2H, $-CH_2-$)

Continued . . .

Table 29 - Continued

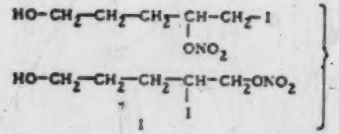
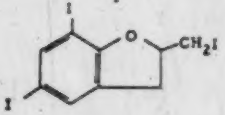
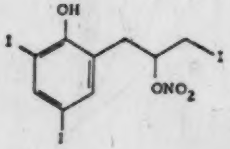
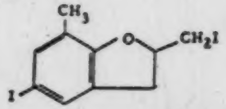
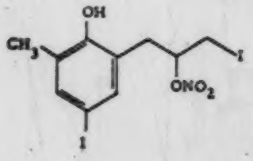
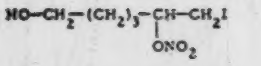
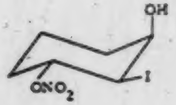
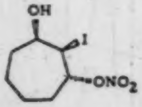
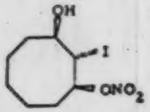
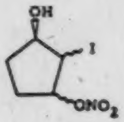
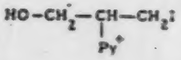
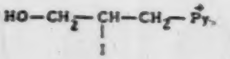
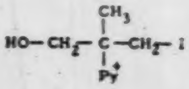
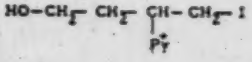
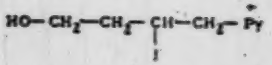
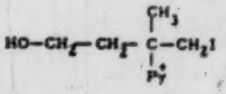
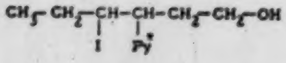
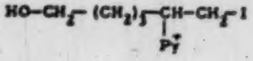
Compounds	$\delta_{TMS}^{CDCl_3}$ -CH-I	-CH-ONO$_2$	-CH$_2$-I	-CH$_2$-ONO$_2$	Additional absorptions
 $HO-CH_2-CH_2-CH_2-\underset{ONO_2}{CH}-CH_2-I$	-	5.03 (0.9H) m	3.42 (1.8H) d J=5	-	1.5-2.2 (m, 4H, 2 -CH$_2$-) 2.82 (s, H, -OH)
$HO-CH_2-CH_2-CH_2-\underset{I}{CH}-CH_2ONO_2$	-	-		4.75 (0.2H) m	3.52 (t, 2H, -CH$_2$OH, J=6 Hz)
	-	-	3.1-3.5 (4H) m	-	4.9 (m, 1H, -CH-O) 7.4, 7.75 (2d, 2H, Aromatic hydrogens, J=1 Hz)
	-	5.0-5.5 (2H) m	3.33 (2H) m	-	3.1 (m, 2H, -CH$_2$-) 7.45, 7.9 (2d, 2H, aromatic hydrogens, J=2 Hz)
	-	-	3.3 (2H) m	-	3.04 (m, 2H, -CH$_2$-) 7.3 (s, 2H, Aromatic hydrogens) 4.8 (m, 1H, -CH-O) 2.14 (s, 3H, - CH$_3$)
	-	5.2 (1H) quint J=6 Hz	3.33 (2H) m	-	2.2 (s, 3H, CH$_3$) 3.1 (m, 2H, CH$_2$) 7.4 (s, 2H, Aromatic hydrogens)

Table 29 - Concluded

Compounds	$\delta_{TMS}^{CDCl_3}$				
	$-CH-I$	$-CH-ONO_2$	$-CH_2-I$	$-CH_2-ONO_2$	Additional absorptions
 $HO-CH_2-(CH_2)_3-\underset{\displaystyle ONO_2}{\underset{\vert}{C}H}-CH_2I$	-	5.00 (1H) m	3.4 (2H) d J=5 Hz	-	1.2-2.1 (m, 6H, 3 $-CH_2-$) 3.00 (s, 1H, $-OH$) 3.63 (t, 2H, $-\underline{CH_2}-OH$, J=5.5 Hz)
	4.48 (1H) q $J_{1,2}$=8.5 Hz $J_{2,3}$=2.5 Hz	5.4 (1H) m	-	-	1.75 (m, 4H, 2 $-CH_2-$) 2.3 (m, 3H, $-CH_2-$, $-OH$) 3.8 (m, 1H, $-\underline{CH}-OH$)
	4.57 (1H) q J=2.25 Hz, 6.75 Hz	5.5 (1H) m	-	-	1.5-2.5 (m, 9H, 4 $-CH_2-$, $-OH$) 3.76 (m, 1H, $-CH-O$)
	4.43 (1H) t J=9 Hz	5.3 (1H) sextet J=9 Hz, 4.5 Hz	-	-	1.6, 2.1 (m, 10H, 5 $-CH_2-$) 3.0 (s, 1H, $-OH$) 4.1 (m, 1H, $-\underline{CH}-OH$)
	4.33 (1H) t J=4.5 Hz	5.6 (1H) m	-	-	1.7-2.8 (m, 5H, 2 $-CH_2-$, $-OH$) 3.83 (s, 1H, $-\underline{CH}-OH$, J=5 Hz)

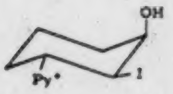
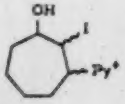
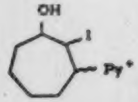
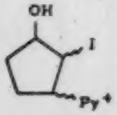
* All these compounds showed -OH and $-ONO_2$ absorptions in the i.r. spectrum between 3400-3600 cm^{-1} and 1620-1640 cm^{-1} respectively.

Table 30. Spectroscopic properties of Hydroxy-iodoalkyl Pyridinium Salts†.

Compound*	δ_{TMS} $(CD_3)_2SO$ -CH–I	-CH–$\overset{+}{N}$<	-CH$_2$–I	-CH$_2$–$\overset{+}{N}$<	Additional absorptions
 $\mathrm{HO{-}CH_2{-}\underset{Py^+}{CH}{-}CH_2I}$		4.5-5.4‡	4.1 (1.5H) d J=5 Hz		3.85 (m, 2H, -$\underline{CH_2}$–OH) 5.83 (s, 1H, –OH)
 $\mathrm{HO{-}CH_2{-}\underset{I}{CH}{-}CH_2{-}\overset{+}{Py}}$					
 $\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{Py^+}{C}}{-}CH_2{-}I}$	-	-	3.8-4.4§ (4H) m		1.95 (s, 3H, –CH$_3$) 5.62 (s, 1H, –OH)
 $\mathrm{HO{-}CH_2{-}CH_2{-}\underset{Py^+}{CH}{-}CH_2{-}I}$	4.8-5.3 m			4.05 m	1.98 (q, 0.68H, -$\underline{CH_2}$–CH–I, J=6 Hz) 2.35(q, 1.32H, -$\underline{CH_2}$–CH–$\overset{+}{N}$<, J=6 Hz) 3.3-3.8 (m, 3.32H, -CH$_2$–I, -$\underline{CH_2}$–OH)
 $\mathrm{HO{-}CH_2{-}CH_2{-}\underset{I}{CH}{-}CH_2{-}\overset{+}{Py}}$					
 $\mathrm{HO{-}CH_2{-}CH_2{-}\overset{CH_3}{\underset{Py^+}{C}}{-}CH_2I}$	-	-	4.1 (2H) q J=11.5 Hz	-	*1.93 (s, 3H, –CH$_3$); 2.4 (t, 2H, -CH$_2$– J=6.5 Hz); 3.5 (t, 2H, -$\underline{CH_2}$–OH, J=6.5 Hz); 4.5 (s, 1H, –OH)
Three  $\mathrm{CH_3{-}CH_2{-}\underset{I}{CH}{-}\underset{Py^+}{CH}{-}CH_2{-}CH_2{-}OH}$	4.7-5.1 (2H) m		-	-	0.73 (t, 3H, -CH$_3$, J=7 Hz); 1.6-2.5 (m, 4H, 2 -CH$_2$–); 3.68 (m, 2H, –$\underline{CH_2}$–OH); 4.3 (s, 1H, –OH)
 $\mathrm{HO{-}CH_2{-}(CH_2)_3{-}\underset{Py^+}{CH}{-}CH_2{-}I}$	-	5.1 (1H) m	4.0 (2H) m	-	0.8-2.4 (m, 6H, 3 –CH$_2$–); 3.4 (m, 2H, –$\underline{CH_2}$–OH); 7.2 (s, 1H, –OH)

Continued . . .

Table 30 - Concluded

Compound *	$\delta_{TMS}^{(CD_3)_2SO}$ -CHI	-CH-$\overset{+}{N}$<	$-CH_2-I$	$-CH_2-\overset{+}{N}$<	Additional absorptions
	5.13 (2H) m		-	-	1.2-2.5 (m, 6H, 3 $-CH_2-$); 3.4 (m, 1H, -CH-OH); 5.8 (d, 1H, -OH, J=8 Hz) 5.8 (d, 1H, -OH, J=8 Hz)
 (1)	5.09 (2H) m		-		1.83, 2.27 (m, 8H, 4 $-CH_2-$); 4.28 (m, 1H, -CH-OH)
 (2)	4.62 (1H) q J=7 Hz, 11 Hz	5.17 (1H) sextet J=11 Hz, 1.5Hz	-	-	1.4-2.4 (m, 8H, 4 $-CH_2-$) 4.08 (m, 1H, -CH-OH)
	4.8 (1H) q J=11 Hz, 4Hz	5.15-5.7 (2H) m			1.8-2.8 (m, 4H, 2 $-CH_2-$) 4.25 (m, 1H, -CH-OH)

* Unless otherwise indicated, the counter-ion was nitrate

† All these compounds had n.m.r. absorption due to $\overset{+}{Py}$ between δ 8-9.5.

‡ Includes $-CH_2-\overset{+}{N}$< hydrogens.

§ Includes $-CH_2-O$ hydrogens.

Table 31. *Erythro* and *Threo*-iodo-nitrate Esters.

Alkene	Iodo-nitrate ester	Boiling Point (°C/mm)	Yield (%)	Formula	Observed % C	Observed % H	Observed % N	Calculated % C	Calculated % H	Calculated % N
E-But-2-ene	*erythro*-3-Iodobut-2-yl nitrate	40/0.05	32	$C_4H_8NO_3I$	19.55	3.31	5.77	19.50	3.26	5.71
Z-But-2-ene	*threo*-3-Iodobut-2-yl nitrate	44/0.03	32	$C_4H_8NO_3I$	19.83	3.25	5.73	19.50	3.26	5.71
E-Pent-2-ene	*erythro*-3-Iodopent-2-yl nitrate *erythro*-2-Iodopent-3-yl nitrate	43-44/0.05	53	$C_5H_{10}NO_3I$	22.69	3.90	5.51	23.18	3.89	5.40
Z-Pent-2-ene	*threo*-3-Iodopent-2-yl nitrate *threo*-2-Iodopent-3-yl nitrate	43-44/0.05	67	$C_5H_{10}NO_3I$	23.20	3.98	5.71	23.18	3.89	5.40
E-4-Methylpent-2-ene	*erythro*-3-Iodo-4-methylpent-2-yl nitrate *erythro*-2-Iodo-4-methylpent-3-yl nitrate	44-45.5/0.04	70	$C_6H_{12}NO_3I$	25.97	4.46	5.17	26.37	4.39	5.13
Z-4-Methylpent-2-ene	*threo*-3-Iodo-4-methylpent-2-yl nitrate	58-58.5/0.02	62	$C_6H_{12}NO_3I$	25.86	4.56	5.26	26.37	4.39	5.13
E-2,2-Dimethylhex-3-ene	*erythro*-4-Iodo-5,5-dimethylhex-3-yl nitrate	58-60/0.02	51	$C_8H_{16}NO_3I$	[†][M-Found 301.0179]			[M-Calc. 301.0179]		
Z-2,2-Dimethylhex-3-ene	*threo*-4-Iodo-5,5-dimethylhex-3-yl nitrate	63-64/0.04	77	$C_8H_{16}NO_3I$	31.81 [M-Found 301.0179]	5.30		31.9 [M-Calc. 301.0179]	5.32	

[†] Determined by mass spectrometry.

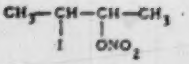
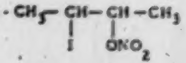
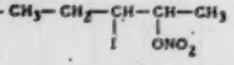
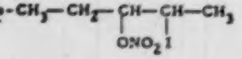
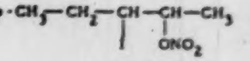
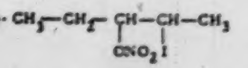
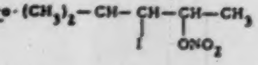
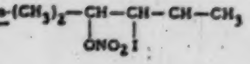
Table 32. Erythro and Threo-Iodopyridinium Salts.

Alkene	Iodopyridinium salt	Melting point (°C)	Yield (%)	Formula	Observed %			Calculated %		
					C	H	N	C	H	N
E-But-2-ene	erythro-N[2-(3-Iodo)butyl]pyridinium nitrate	Oil	55*	-	-	-	-	-	-	-
Z-But-2-ene	threo-N[2-(3-Iodo)butyl]pyridinium nitrate	108-112	54	$C_9H_{13}N_2O_3I$	33.17	4.13	8.74	33.34	4.01	8.64
E-Pent-2-ene	erythro-N-[2-(3-Iodo)pentyl]pyridinium nitrate	96-99	12	$C_{10}H_{15}N_2O_3I$	35.88	4.67	8.60	35.50	4.44	8.28
Z-Pent-2-ene	threo-N-[2-(3-Iodo)pentyl] pyridinium nitrate threo-N-[3-(2-Iodo)pentyl] pyridinium nitrate	94-97	6	$C_{10}H_{15}N_2O_3I$	36.81	4.54	-	35.50	4.44	-
E-4-Methylpent-2-ene	erythro-N-[2-(3-Iodo-4-methyl)pentyl] pyridinium nitrate	125-128	15	$C_{11}H_{17}N_2O_3I$	37.60	5.04	7.92	37.51	4.83	7.95
Z-4-Methylpent-2-ene	threo-N-[2-(3-Iodo-4-methyl)pentyl]-pyridinium nitrate	84-87	14	$C_{11}H_{17}N_2O_3I$	37.49	4.79	8.49	37.51	4.83	7.95
E-3-Methylpent-2-ene	threo-N-[3-(2-Iodo-3-methyl)pentyl]-pyridinium nitrate	126-129	39	$C_{11}H_{17}N_2O_3I$	37.04	4.84	-	37.51	4.83	-
Z-3-Methylpent-2-ene	erythro-N-[3-(2-Iodo-3-methyl)pentyl]-pyridinium nitrate	Oil	43†	-	-	-	-	-	-	-
E-Stilbene	erythro-N-[1-(2-Iodo-1,2-diphenyl)ethyl]-pyridinium nitrate	144-145	62	$C_{19}H_{17}N_2O_3I$	50.84	3.80	6.34	50.89	3.80	6.25
E-Stilbene	E-N-(1,2-Diphenylethenyl)pyridinium iodide	242-245	86	$C_{19}H_{16}NI$	59.46	4.29	3.78	59.21	4.16	3.64
Z-Stilbene	Z-N-(1,2-Diphenylethenyl)pyridinium iodide	264-266	83	$C_{19}H_{16}NI$	59.30	4.24	3.77	59.21	4.16	3.64

* Not obtained in analytically pure form. Characterized by its elimination product.

† Not obtained in analytically pure form.

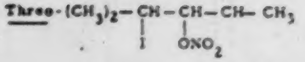
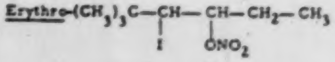
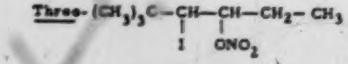
Table 33. Spectroscopic Properties of Erythro and Threo-iodo-nitrate Esters. *

Compound	$\delta_{TMS}^{CDCl_3}$			
	$-CH-I$	$-CH-ONO_2$	J_{CH-CH} (Hz)	Additional absorptions
Erythro-  $CH_3-CH(I)-CH(ONO_2)-CH_3$	4.23 (1H) octet	4.69 (1H) octet	5.1	1.39 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.2 Hz) 1.83 (d, 3H, $\underline{CH}_3$-CH-I, J=7.1 Hz)
Threo-  $CH_3-CH(I)-CH(ONO_2)-CH_3$	4.29 (1H) octet	5.07 (1H) octet	4.0	1.47 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.2 Hz) 1.88 (d, 3H, $\underline{CH}_3$-CH-I, J=7.1 Hz)
Erythro-  $CH_3-CH_2-CH(I)-CH(ONO_2)-CH_3$	4.09-4.45 (1H) m	4.68-4.92 (1H) m		1.07 (t, 2.07H, $\underline{CH}_3$-CH$_2$-, J=7.1 Hz); 1.48 (d, 2.07H, $\underline{CH}_3$-CH-ONO$_2$, J=6.2 Hz); 1.77 (q, 2H, -CH$_2$-, J=7.1 Hz)
Erythro-  $CH_3-CH_2-CH(ONO_2)-CH(I)-CH_3$				1.03 (t, 0.93H, $\underline{CH}_3$-CH$_2$-, J=7.1 Hz) 1.91 (d, 0.93H, $\underline{CH}_3$-CH-I, J=6.1 Hz)
Threo-  $CH_3-CH_2-CH(I)-CH(ONO_2)-CH_3$	4.1 (0.7H) sextet	5.15 (0.7H) octet	4.0	1.06 (t, 2.1H, $\underline{CH}_3$-CH$_2$-, J=7 Hz); 1.51 (d, 2.1H, $\underline{CH}_3$-CH-ONO$_2$, J=6.5 Hz); 1.82 (q, 2H, -CH$_2$-, J=7 Hz)
Threo-  $CH_3-CH_2-CH(ONO_2)-CH(I)-CH_3$	4.33 (0.3H) octet	4.81 (0.3H) quint	4.0	1.0 (t, 0.9H, $\underline{CH}_3$-CH$_2$-, J=7 Hz) 1.89 (d, 0.9H, $\underline{CH}_3$-CH-I, J=6.1 Hz)
Erythro-  $(CH_3)_2-CH-CH(I)-CH(ONO_2)-CH_3$	4.20 (0.8H) q	5.08 (1H) sextet	7.0	1.0 (m, 3H, ($\underline{CH}_3$)$_2$-CH-); 1.59 (d, 2.4H, $\underline{CH}_3$-CH ONO$_2$, J=6 Hz); 1.52 (m, 0.8H, -$\underline{CH}$-(CH$_3$)$_2$);
Erythro-  $(CH_3)_2-CH(ONO_2)-CH(I)-CH-CH_3$	4.25 (0.2H) quint		7.0	1.95 (d, 0.6H, $\underline{CH}_3$-CH-I, J=7 Hz); 2.4 (m, 0.2H, -$\underline{CH}$(CH$_3$)$_2$

Continued . . .

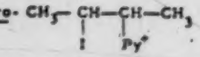
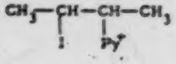
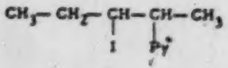
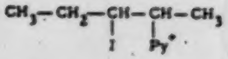
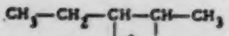
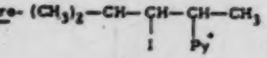
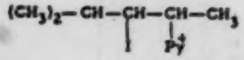
Table 33 - Concluded

Table

Compound	δ_{TMS} $CDCl_3$			
	$-CH-I$	$-CH-ONO_2$	J_{CH-CH} (Hz)	Additional absorptions
 **Threo**- $(CH_3)_2-\underset{I}{CH}-\underset{ONO_2}{CH}-CH-CH_3$	4.04 (1H) q	5.1 (1H) quint	5.3	1.03 (d, 3H, $(\underline{CH_3})_2$-CH, J=6.2 Hz) 1.05 (d, 3H, $(\underline{CH_3})_2$-CH, J=6.2 Hz) 1.40 (m, 1H, -$\underline{CH}(CH_3)_2$, J=4 Hz) 1.49 (d, 3H, $\underline{CH_3}$-CH-ONO_2, J=6.3 Hz)
 **Erythro**-$(CH_3)_3C-\underset{I}{CH}-\underset{ONO_2}{CH}-CH_2-CH_3$	4.32 (1H) q	4.6 (1H) octet	2.75	1.06 (t, 3H, $\underline{CH_3}$-CH_2, J=7.7 Hz) 1.18 (s, 9H, $(CH_3)_3C$-) 1.70-1.93 (m, 2H, -CH_2-)
 **Threo**- $(CH_3)_3C-\underset{I}{CH}-\underset{ONO_2}{CH}-CH_2-CH_3$	4.05 (1H) d	4.71 (1H) sextet	1.5	0.98 (t, 3H, $\underline{CH_3}$-CH_2, J=8 Hz) 1.35 (s, 9H, $(CH_3)_3$-C) 1.89-2.21 (m, 2H, -CH_2-, J_{CH_2-CH-}=6.5 Hz)

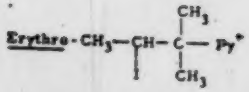
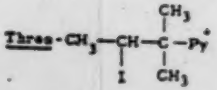
* All these compounds exhibited ONO_2 i.r. absorption between 1620 and 1640 cm^{-1}.

Table 34. Spectroscopic Properties of *Erythro* and *Threo*-iodo-pyridinium nitrates.*†

Compound	δ_{TMS} $(CD_3)_2SO$ $-CH-I$, $-CH-\overset{+}{N}<$	Additional absorptions
Erythro-  $CH_3-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$	4.6-5.35 (2H) m	1.83 (two overlapping doublets, 6H, 2 $-CH_3$)
Threo-  $CH_3-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$	4.5-5.4 (2H) m	1.7 (d, 3H, $\underline{CH}_3$-CH-I, J=6.5 Hz) 1.92 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=6.5 Hz)
Erythro-  $CH_3-CH_2-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$	4.4-5.5 (2H) m	1.02 (t, 3H, $\underline{CH}_3$-CH_2-, J=6.5 Hz) 1.76 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=6.5 Hz) 1.8 (m, 2H, -CH_2-)
Threo-  $CH_3-CH_2-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$ **Threo-**  $CH_3-CH_2-\underset{Py^+}{CH}-\underset{I}{CH}-CH_3$	4.4-5.4 (2H) m	0.7-1.2 (two overlapping triplets, 3H, $\underline{CH}_3$-CH_2-) 1.75 (d, $\underline{CH}_3$-CH-$\overset{+}{N}<$) 1.9 (m, 2H, -CH_2-)
Erythro-  $(CH_3)_2-CH-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$	4.7-5.4 (2H) m	0.9 (m, 7H, $(\underline{CH}_3)_2$-$\underline{CH}$-) 1.9 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=6.2 Hz)
Threo-  $(CH_3)_2-CH-\underset{I}{CH}-\underset{Py^+}{CH}-CH_3$	4.7-5.65 (2H) m	0.73 (two overlapping doublets, 6H, $(\underline{CH}_3)_2$-CH-) 1.17 (m, 1H, -$\underline{CH}(CH_3)_2$) 1.8 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=6.5 Hz)

Continued . . .

Table 34 - Concluded

Compound	δ_{TMS} $(CD_3)_2CO$		
	$-CH-I$	$-CH-\overset{+}{N}<$	Additional absorptions
 $\underline{Erythro}-CH_3-\underset{I}{CH}-\overset{CH_3}{\underset{CH_3}{C}}-Py^{*}$	5.02 (1H) q J=7 Hz		0.72 (t, 3H, $\underline{CH_3}-CH_2$, J=7 Hz) 1.7 (d, 3H, CH_3-CH-I, J=7 Hz) 1.98 (s, 3H, $\underline{CH_3}-C-\overset{+}{N}<$) 2.33 (m, 2H, $-CH_2-$)
 $\underline{Threo}-CH_3-\underset{I}{CH}-\overset{CH_3}{\underset{CH_3}{C}}-Py^{+}$	5.18 (1H) q J=6.8 Hz		0.65 (t, 3H, $\underline{CH_3}CH_2-$, J=7 Hz) 1.93 (s, 3H, $\underline{CH_3}-C-\overset{+}{N}<$) 2.05 (d, 3H, $\underline{CH_3}-CH-I$, J=6.8 Hz) 2.3 (m, 2H, $-CH_2-$)

* All these compounds had $\cdot NO_2^-$ absorption between 1620 and 1640 cm^{-1} (i.r. KBr disc).

† All these compounds had n.m.r. absorption due to Py^{+} between δ 8-9.5.

Table 35. Bromo-nitrate Esters.

Alkene	Bromo-nitrate ester	Boiling point (°C/mm)	Yield (%)	Formula	Observed %				Calculated %			
					C	H	N	Br	C	H	N	Br
Hex-1-ene	1-Bromohex-2-yl nitrate 2-Bromohex-1-yl nitrate	57-58/0.05	49	$C_6H_{12}NO_3Br$	31.89	5.30	6.36	35.99	31.85	5.31	6.19	35.40
3,3-Dimethylbut-1-ene	2-Bromo-3,3-dimethylbutyl nitrate	54-55/0.05	51.5	$C_6H_{12}NO_3Br$	31.87	5.33	6.10	35.36	31.85	5.31	6.19	35.40
Z-Pent-2-ene	threo-3-Bromopent-2-yl nitrate threo-2-Bromopent-3-yl nitrate	32-33/0.06	53.0	$C_5H_{10}NO_3Br$	28.37	4.75	6.45	37.72	28.31	4.72	6.6	37.74
E-4,4-Dimethyl-pent-2-ene	erythro-3-Bromo-4,4-dimethylpent-2-yl nitrate	53/0.02	80.0	$C_7H_{14}NO_3Br$	35.02	5.74	5.75	33.42	35.00	5.82	5.82	33.34
2-Methylbut-2-ene	3-Bromo-2-methylbut-2-yl nitrate	30/0.3	35.0	$C_5H_{10}NO_3Br$	28.43	4.93	6.47	-	28.32	4.75	6.60	-
Cyclohexene	2-Bromocyclohexyl nitrate	67/0.05	52.0	$C_6H_{10}NO_3Br$	32.36	4.56	6.14	35.65	32.15	4.47	6.25	35.72
Norbornene*	2-Bromonorborn-3-yl nitrate	73/0.03	15.0	$C_7H_{10}NO_3Br$	35.32	4.29	-	-	35.59	4.24	-	-
Norbornadiene	Tricyclo[2.2.1.0^{2,6}]-5-bromohept-3-yl nitrate 3-Bromo-5-norbornen-2-yl nitrate	57/0.05	45.0	$C_7H_8NO_3Br$	35.99	3.50	5.56	34.28	35.90	3.42	5.98	34.20
1,4-Cyclohexadiene	5-Bromocyclohexen-4-yl nitrate	56/0.05	54.0	$C_8H_8NO_3Br$	32.06	3.59	6.22	-	32.43	3.60	6.30	-
4-Vinylcyclohex-1-ene	2(1)-Bromo-4-vinylcyclohexyl nitrate	63/0.05	35.0	$C_8H_{12}NO_3Br$	38.50	4.79	5.31	32.18	38.41	4.80	5.60	32.00
2,4-Hexadiene	5-Bromohex-3-en-2-yl nitrate	58-59/0.05	19.0	$C_6H_{10}NO_3Br$	31.95	4.44	6.07	36.11	32.15	4.47	6.25	35.72
2,3-Dimethyl-1,3-butadiene	4-Bromo-2,3-dimethylbut-2-en-1-yl nitrate	57-58/0.05	31.0	$C_6H_{10}NO_3Br$	31.84	4.43	6.32	35.75	32.15	4.47	6.25	35.72
Styrene	2-Bromo-1-phenylethyl nitrate	80/0.03	49.0	$C_8H_8NO_3Br$	39.24	3.24	5.44	32.93	39.03	3.25	5.69	32.53
Z-But-2-ene	threo-3-Bromobut-2-yl nitrate	23/0.05	48.0	$C_4H_8NO_3Br$	23.98	3.98	6.78	40.79	24.24	4.04	7.07	40.40
E-But-2-ene	erythro-3-Bromobut-2-yl nitrate	25/0.03	44.0	$C_4H_8NO_3Br$	24.24	4.07	7.01	40.33	24.24	4.04	7.07	40.40
Z-4-Methylpent-2-ene	threo-3-Bromo-4-methylpent-2-yl nitrate	30/0.07	58.0	$C_6H_{12}NO_3Br$	32.02	5.42	6.26	35.77	31.85	5.31	6.19	35.40

Continued . . .

Table 35 - Concluded

Alkene	Bromo-nitrate ester	Boiling point (°C/mm)	Yield (%)	Formula	Observed % C	Observed % H	Observed % N	Observed % Br	Calculated % C	Calculated % H	Calculated % N	Calculated % Br
E-4-Methylpent-2-ene	erythro-3-Bromo-4-methylpent-2-yl nitrate erythro-2-Bromo-4-methylpent-3-yl nitrate	27/0.07	61.0	$C_6H_{12}NO_3Br$	32.03	5.41	6.12	36.22	31.85	5.31	6.19	35.40
Z-Stilbene	threo-2-Bromo-1,2-diphenylethyl nitrate	87-88[†]	52.0	$C_{14}H_{12}NO_3Br$	51.63	3.74	4.37	-	52.17	3.73	4.35	-
E-Stilbene	erythro-2-Bromo-1,2-diphenylethyl nitrate	144-145[†]	21.0	$C_{14}H_{12}NO_3Br$	52.21	3.78	4.12	24.68	52.17	3.73	4.35	24.83
Allyl alcohol	3-Hydroxy-1-bromoprop-2-yl nitrate 3-Hydroxy-2-bromoprop-1-yl nitrate	70/0.05	31.0	$C_3H_6NO_4Br$	18.56	3.06	6.53	39.95	18.00	3.00	7.00	40.00
But-3-en-1-ol	4-Hydroxy-1-bromobut-2-yl nitrate 4-Hydroxy-2-bromobut-1-yl nitrate[*]	-	33.0		-	-	-	-	-	-	-	-
Pent-4-en-1-ol	5-Hydroxy-1-bromopent-2-yl nitrate 5-Hydroxy-2-bromopent-1-yl nitrate	-	29.0		-	-	-	-	-	-	-	-
Cyclohex-2-en-1-ol	3-Hydroxy-2-bromocyclohexyl nitrate 6-Hydroxy-2-bromocyclohexyl nitrate	81-82/0.02	52.0	$C_6H_{10}NO_4Br$	29.85	4.14	5.26	33.45	30.00	4.17	5.82	33.34

[*] Nortricyclanyl bromide was produced in 50% yield.

[†] Melting point (hexane).

Table 36. Bromo-pyridinium Salts.

Alkene	Bromo-pyridinium salt	Melting point (°C)	Yield (%)	Formula	Observed %				Calculated %			
					C	H	N	Br	C	H	N	Br
Hex-1-ene	N-[2-(1-Bromohexyl)] pyridinium nitrate N-[1-(2-Bromohexyl)] pyridinium nitrate	Oil	34	-	-	-	-	-	-	-	-	-
3,3-Dimethylbut-1-ene	N-[1-(2-Bromo-3,3-dimethylbutyl] pyridinium nitrate	126-127	30	$C_{11}H_{17}N_2O_3Br$	43.28	5.62	9.09	26.25	43.28	5.57	9.18	26.23
Z-Pent-2-ene	threo-N-[2-(3-Bromopentyl)] pyridinium nitrate threo-N-[3-(2-Bromopentyl)] pyridinium nitrate	Oil	27.5	-	-	-	-	-	-	-	-	-
2-Methylbut-2-ene	N-[2-(2-Methyl-3-bromobutyl)] pyridinium nitrate	117-118	20	$C_{10}H_{15}N_2O_3Br$	40.83	5.27	9.20	-	41.25	5.19	9.62	-
Ethyl vinyl ether	N-[1-(1-Ethoxy-2-bromoethyl)] pyridinium nitrate	Oil	70	-	-	-	-	-	-	-	-	-
Cyclohexene	N-(2-Bromocyclohexyl)pyridinium nitrate	135-136	31.5	$C_{11}H_{15}N_2O_3Br$	43.49	5.00	9.11	26.23	43.57	4.95	9.24	26.40
Norbornadiene	N-[3-(5-Bromonortricyclanyl)] pyridinium nitrate	174-177	12	$C_{12}H_{13}N_2O_3Br$	45.85	4.19	8.87	25.30	46.02	4.15	8.99	25.57
1,4-Cyclohexadiene	N-[4-(5-Bromocyclohexenyl)] pyridinium nitrate	132-134	25	$C_{11}H_{13}N_2O_3Br$	43.66	4.33	9.07	26.58	43.85	4.32	9.30	26.58
4-vinylcyclohex-1-ene	N-[1(2)-2(1)-Bromo-4-vinylcyclohexyl)]-pyridinium nitrate	Oil	40.0		-	-	-	-	-	-	-	-
2,4-Hexadiene	N-[4-(5-Bromohex-2-enyl)] pyridinium nitrate N,N'-[2,5-(Hex-3-enyl)] dipyridinium nitrate, bromide	Oil	70		-	-	-	-	-	-	-	-
2,3-Dimethyl-1,3-butadiene	N-[3-(4-Bromo-2,3-dimethylbutenyl)]-pyridinium nitrate	Oil	34		-	-	-	-	-	-	-	-
	N,N'-[1,4-(2,3-Dimethylbut-2-enyl)]-dipyridinium nitrate, bromide	238-240 (dec)	16		50.73	5.31	-	-	50.25	5.24	-	-

Continued . . .

Table 16 - Continued

Alkene	Bromo-pyridinium salt	Melting Point (°C)	Yield (%)	Formula	Observed %				Calculated %			
					C	H	N	Br	C	H	N	Br
Dihydropyran	N-(3-Bromotetrahydropyranosyl)pyridinium nitrate	117-118	45	$C_{10}H_{13}N_2O_4Br$	39.29	4.31	9.10	26.62	39.34	4.26	9.18	26.23
Styrene	N-[1-(1-Phenylethenyl)]pyridinium bromide	80	26.5	-	-	-	-	-	-	-	-	-
Z-But-2-ene	threo-N-[2-(3-Bromobutyl)]pyridinium nitrate	Oil	29	-	-	-	-	-	-	-	-	-
E-But-2-ene	erythro-N-[2-(3-Bromobutyl)]pyridinium nitrate	Oil	37	-	-	-	-	-	-	-	-	-
Z-4-Methylpent-2-ene	threo-N[2-(3-Bromo-4-methylpentyl)]-pyridinium nitrate	70-75	18	$C_{11}H_{17}N_2O_3Br$	41.99	5.49	8.87	26.32	43.28	5.57	9.18	26.23
E-4-Methylpent-2-ene	erythro-N-[2-(3-Bromo-4-methylpentyl)]-pyridinium nitrate erythro-N-[3-(2-Bromo-4-methylpentyl)]-pyridinium nitrate	108-110	21	$C_{11}H_{17}N_2O_3Br$	42.48	5.49	8.73	26.79	43.28	5.57	9.18	26.23
Z-Stilbene	threo-N-[1-(2-Bromo-1,2-diphenylethyl)]-pyridinium nitrate	168-171	32	$C_{19}H_{17}N_2O_3Br$	55.43	4.29	6.95	19.49	56.85	4.24	6.98	19.95
E-Stilbene†	erythro-N-[1-(2-Bromo-1,2-diphenylethyl)]-pyridinium nitrate	174-176	63.5	$C_{19}H_{17}N_2O_3Br$	56.83	4.28	6.74	19.88	56.85	4.24	6.98	19.95
Allyl alcohol	N-[2-(3-Hydroxy-1-bromopropyl)]-pyridinium nitrate N-[1-(3-Hydroxy-2-bromopropyl)]-pyridinium nitrate	Oil	37	-	-	-	-	-	-	-	-	-
But-3-en-1-ol	N-[2-(4-Hydroxy-1-bromobutyl)]-pyridinium nitrate N-[1-(4-Hydroxy-2-bromobutyl)]-pyridinium nitrate	Oil	55	-	-	-	-	-	-	-	-	-

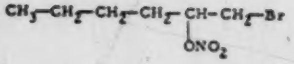
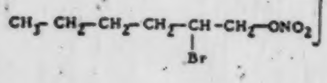
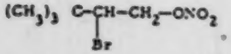
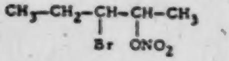
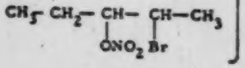
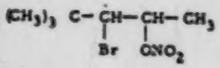
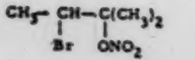
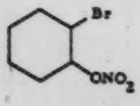
Continued . . .

Table 36 - Concluded

Alkene	Bromo-pyridinium salt	Melting point (°C)	Yield (%)	Formula	Observed %				Calculated %			
					C	H	N	Br	C	H	N	Br
Pent-4-en-1-ol	N-[2-(5-Hydroxy-1-bromopentyl)]-pyridinium nitrate N-[1-(5-HYdroxy-2-bromopentyl)]-pyridinium nitrate	Oil	20		-	-	-	-	-	-	-	-
Cyclohex-2-en-1-ol	†	172-177	23.5	$C_{11}H_{15}N_2O_4Br$	41.20	4.78	8.61	24.49	41.38	4.70	8.78	25.1

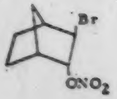
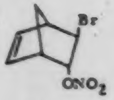
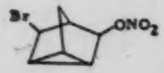
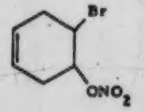
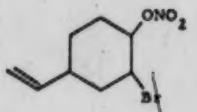
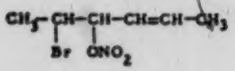
† The n.m.r. spectrum shows more than one compound. It was difficult to assign any structure.

Table 37. Spectroscopic Properties of Bromo-nitrate Esters.†

Compound	$\delta_{TMS}^{CDCl_3}$				Additional absorptions
	$-\underset{\mid}{C}H-Br$	$-CH-ONO_2$	$-CH_2-Br$	$-CH_2-ONO_2$	
 $CH_3-CH_2-CH_2-CH_2-\underset{ONO_2}{\underset{\mid}{CH}}-CH_2-Br$	-	5.2 (0.67H) quint J=5.5 Hz	3.55 (1.34H) d J=5.5 Hz		0.7-2.1 (m, 9H, $-CH_2-$, $-CH_3$)
 $CH_3-CH_2-CH_2-CH_2-\underset{Br}{\underset{\mid}{CH}}-CH_2-ONO_2$	4.15 (0.33H) m	-	-	4.7 (0.66H) t	
 $(CH_3)_3\ C-\underset{Br}{\underset{\mid}{CH}}-CH_2-ONO_2$	4.02 (1H) m	-	-	4.7 (2H) m	1.3 (s, 9H, $(CH_3)_3-C$)
Threo  $CH_3-CH_2-\underset{Br}{\underset{\mid}{CH}}-\underset{ONO_2}{\underset{\mid}{CH}}-CH_3$	4.00 (0.64H) quint J=4.5 Hz	5.31 (0.64H) octet J=4.5, 6.5 Hz	-	-	1.06 (q, 3H, $\underline{CH_3}-CH_2-$, J=6.5 Hz) 1.49 (d, 1.92H, $\underline{CH_3}-CH-ONO_2$, J=6.5 Hz)
Threo  $CH_3-CH_2-\underset{ONO_2}{\underset{\mid}{CH}}-\underset{Br}{\underset{\mid}{CH}}-CH_3$	4.25 (0.36H) octet J=4.5, 7 Hz	5.07 (0.36H) quint J=4.5 Hz	-	-	1.71 (d, 1.08H, $\underline{CH_3}-CH-Br$, J=7 Hz) 1.85 (m, 2H, $-CH_2-$)
Erythro  $(CH_3)_3\ C-\underset{Br}{\underset{\mid}{CH}}-\underset{ONO_2}{\underset{\mid}{CH}}-CH_3$	4.2 (1H) d J=2.5 Hz	5.37 (1H) octet J=2.5, 7.5 Hz	-	-	1.15 (s, 9H, $(CH_3)_3-C-$) 1.55 (d, 3H, $\underline{CH_3}-CH-ONO_2$, J=7.5 Hz)
 $CH_3-\underset{Br}{\underset{\mid}{CH}}-\underset{ONO_2}{\underset{\mid}{C}}(CH_3)_2$	4.7 (1H) q J=7 Hz	-	-	-	1.65-1.77 (s, d, 9H, 3 $-CH_3$)
	4.03 (1H) sextet J=9, 4.5 Hz	5.1 (1H) m	-	-	1-2.6 (m, 8H, 4 $-CH_2-$)

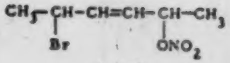
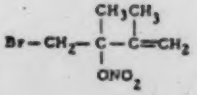
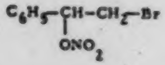
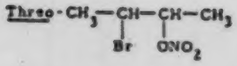
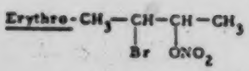
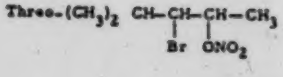
Continued . . .

Table 37 - Continued

Compound	$\delta_{TMS}^{CDCl_3}$				Additional absorptions
	$-CH-Br$	$-CH-ONO_2$	$-CH_2-Br$	$-CH_2-ONO_2$	
	3.93 (1H) m	4.9 (1H) m	-	-	1.1-2.8 (m, 8H, 2 -CH-, 3 -CH$_2$-)
	4.1 (0.36H) m	4.95 (1H) m	-	-	1.4-2.6 (m, 4.56H, -CH$_2$-, 2.56 -CH-) 3.15 (m, 0.72 H, -CH-CH=CH-CH-) 6.3 (m, 0.72H, olefinic hydrogens)
	4.42 (0.64H) m				
	4.30 (1H) m	5.4 (1H) m	-	-	2.1-3.2 (m, 4H, 2 -CH$_2$-) 5.7 (m, 2H, olefinic hydrogens)
	4.4 (1H) m	5.25 (1H) m	-	-	1.4-2.8 (m, 7H, 3 -CH$_2$-, 1 -CH-) 4.85-6.1(m, 4H, olefinic hydrogens, -CH-ONO$_2$)
 $CH_3-\underset{Br}{\underset{\mid}{CH}}-\underset{ONO_2}{\underset{\mid}{CH}}-CH=CH-CH_3$	4.24 (1H) octet J=7, 4 Hz	5.26-6.2* (3H) m			1.8 (m, 6H, 2 -CH$_3$)

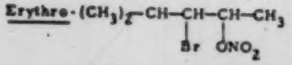
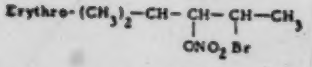
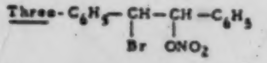
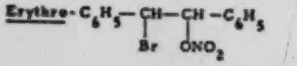
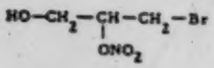
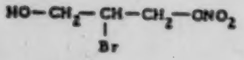
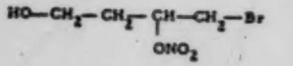
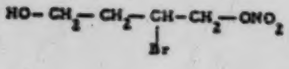
Continued . . .

Table 37. - Continued

Compound	δ_{TMS} $CDCl_3$				Additional absorptions
	-CH-Br	-CH-ONO$_2$	-CH$_2$-Br	-CH$_2$-ONO$_2$	
 $CH_3-\underset{Br}{CH}-CH=CH-\underset{ONO_2}{CH}-CH_3$	4.65 (1H) quint J=7 Hz	5.5 (1H) m	-	-	1.43 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.5 Hz) 1.78 (d, 3H, $\underline{CH}_3$-CH-Br, J=7 Hz) 5.92 (m, 2H, olefinic hydrogens)
 $Br-CH_2-\overset{CH_3}{\underset{ONO_2}{C}}-\overset{CH_3}{C}=CH_2$	-	-	3.55, 3.85 (2H) 2d J=11 Hz		1.73 (s, 3H, $CH_3-\overset{\mid}{\underset{\mid}{C}}-$) 1.82 (m, 3H, $CH_3-\overset{\mid}{C}=$) 5.12 (m, 2H, olefinic hydrogens)
$Br-CH_2-C(CH_3)=C(CH_3)-CH_2ONO_2$	-		3.97, 4.04 (2H) 2s	4.95, 4.98 (2H) 2s	1.8-1.93 (m, 6H, 2 -CH$_3$)
 $C_6H_5-\underset{ONO_2}{CH}-CH_2-Br$	-	6.00 (1H) q J=6, 7.5 Hz	3.62 (2H) t J=6, 7.5 Hz		7.37 (s, 5H, aromatic hydrogens)
 Threo-$CH_3-\underset{Br}{CH}-\underset{ONO_2}{CH}-CH_3$	4.26 (1H) octet J=4.5, 7 Hz	5.12 (1H) octet J=4.5, 6.5 Hz	-	-	1.45 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.5 Hz) 1.70 (d, 3H, $\underline{CH}_3$-CH-Br, J=7 Hz)
 Erythro-$CH_3-\underset{Br}{CH}-\underset{ONO_2}{CH}-CH_3$	1.25 (1H) octet J=4.5, 7 Hz	5.1 (1H) octet J=4.5, 6.5 Hz	-	-	1.45 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.5 Hz) 1.70 (d, 3H, $\underline{CH}_3$-CH-Br, J=7 Hz)
 Threo-$(CH_3)_2\ CH-\underset{Br}{CH}-\underset{ONO_2}{CH}-CH_3$	3.89 (1H) q J=6.5, 5Hz	5.07 (1H) quint J=6.5 Hz	-	-	1.02-1.12 (2d, 6H, $(\underline{CH}_3)_2$-CH) 1.48 (d, 3H, $\underline{CH}_3$-CH-ONO$_2$, J=6.5 Hz) 2.00 (m, 1H, -$\underline{CH}$-(CH$_3$)$_2$)

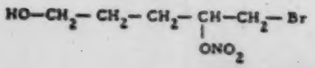
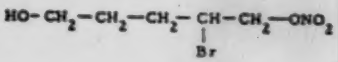
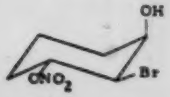
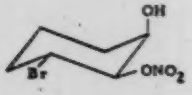
Continued . . .

Table 37 - Continued

Compound		$\delta_{TMS}^{CDCl_3}$			
	$-CH-Br$	$-CH-ONO_2$	$-CH_2-Br$	$-CH_2-ONO_2$	Additional absorptions
 **Erythro**-$(CH_3)_2-CH-CH(Br)-CH(ONO_2)-CH_3$	4.00 (0.74H) q J=6.5, 5 Hz)	5.24 (1H) quint J=6 Hz	-	-	0.96-1.10 (m, 6H, $\underline{(CH_3)}_2$-CH-) 1.54 (d, 2.22H, $\underline{CH}_3$-CH-ONO_2, J=6.5 Hz) 1.70 (d, 0.78H, $\underline{CH}_3$-CH-Br, J=6.5 Hz) 1.9-2.4 (m, 1H, -$\underline{CH}$-$(CH_3)_2$)
 Erythro-$(CH_3)_2-CH-CH(ONO_2)-CH(Br)-CH_3$	4.24 (0.26H) quint J=6.5 Hz				
 **Threo**-$C_6H_5-CH(Br)-CH(ONO_2)-C_6H_5$	5.11 (1H) d J=9.2 Hz	6.21 (1H) d J=9.2 Hz	-	-	7.12 (m, 10H, aromatic hydrogens).
 **Erythro**-$C_6H_5-CH(Br)-CH(ONO_2)-C_6H_5$	5.13 (1H) d J=8 Hz	6.28 (1H) d J=8 Hz	-	-	7.3 (m, 10H, aromatic hydrogens)
 $HO-CH_2-CH(ONO_2)-CH_2-Br$ *	-	5.30 (0.69H) quint J=6 Hz	3.63 (1.38H) d J=6 Hz	-	3.5 (s, 1H, -O-H) 3.97 (d, 2H, $\underline{CH}_2$-OH, J=5 Hz)
 $HO-CH_2-CH(Br)-CH_2-ONO_2$	4.3 (0.31H) m			4.83 (0.62H) d J=6 Hz	
 $HO-CH_2-CH_2-CH(ONO_2)-CH_2-Br$ *	-	5.42 (0.67H) m	3.63 (1.34H) d J=5.5 Hz		2.05 (q, 2H, -CH_2-, J=6 Hz) 2.73 (s, 1H, O-H) 3.65 (m, 2H, -$\underline{CH}_2$-OH)
 $HO-CH_2-CH_2-CH(Br)-CH_2-ONO_2$	4.3 (0.33H) m			4.62 (0.66H) m	

Continued . . .

Table 37 - Concluded

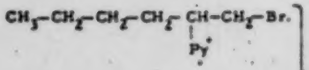
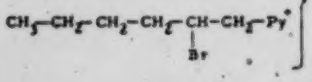
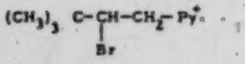
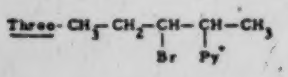
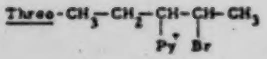
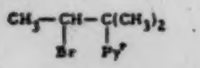
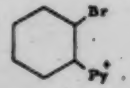
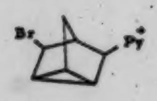
Compound	$\delta_{TMS}^{CDCl_3}$ -CH-Br	-CH-ONO$_2$	-CH$_2$-Br	-CH$_2$-ONO$_2$	Additional absorptions
 $HO-CH_2-CH_2-CH_2-\underset{ONO_2}{\underset{\vert}{CH}}-CH_2-Br$ ‡		5.25 (0.67H) m	3.55 (1.34H) d J=5 Hz		1.5-2.3 (m, 5H, 2 -CH$_2$-, -OH) 3.70 (t, 2H, -CH$_2$-OH, J=5 Hz)
 $HO-CH_2-CH_2-CH_2-\underset{Br}{\underset{\vert}{CH}}-CH_2-ONO_2$	4.15 (0.33H) m			4.72 (0.66H) t J=5, 7 Hz	
	4.2 (0.625H) q $J_{a,e}$=3 Hz $J_{a,a}$=8.5 Hz	5.41 (0.625H) sextet $J_{a,e}$=4 Hz $J_{a,a}$=8.5 Hz	-	-	1.20-2.4 (m, 6H, 3 -CH$_2$-) 2.74 (s, 1H, -OH) 3.5-4.5 (m, 2H, CH-OH, -CH-Br)
		5.14 (?H) q $J_{a,e}$=3 Hz $J_{a,a}$=8.5 Hz	-	-	

† All these compounds had -ONO$_2$ i.r. absorption between 1620 and 1640 cm^{-1}.

‡ All these compounds showed -OH i.r. absorption between 3300 and 3600 cm^{-1}.

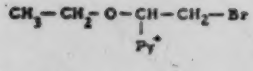
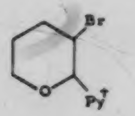
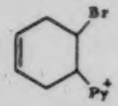
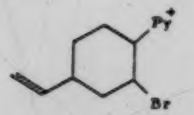
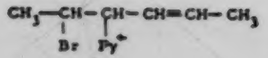
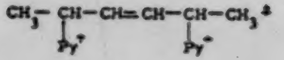
• Includes two olefinic hydrogens.

Table 38. Spectroscopic Properties of Bromo-pyridinium Salts.*

Compounds †	δ_{TMS} $(CD_3)_2SO$ -CH-Br	-CH-$\overset{+}{N}$<	-CH_2-Br	-CH_2-$\overset{+}{N}$<	Additional absorptions
 $CH_3-CH_2-CH_2-CH_2-\underset{Py^+}{CH}-CH_2-Br$  $CH_3-CH_2-CH_2-CH_2-\underset{Br}{CH}-CH_2-Py^+$		4.8-5.55 (1H) m	4.3 (1.3H) t J=6, 8 Hz	4.8 (0.7H) m	0.6-2.5 (m, 9H, 3 -CH_2-, -CH_3)
 $(CH_3)_3\ C-\underset{Br}{CH}-CH_2-Py^+$	5.4 (1H) t J=10 Hz	-	-	4.65-5.2 (2H) m	1.2 (s, 9H, $(CH_3)_3$-C-)
 Threo- $CH_3-CH_2-\underset{Br}{CH}-\underset{Py^+}{CH}-CH_3$  Threo- $CH_3-CH_2-\underset{Py^+}{CH}-\underset{Br}{CH}-CH_3$		4.65-5.6 (2H) m	-	-	0.75 (t, 0.9H, $\underline{CH}_3$-CH_2-CH-$\overset{+}{N}$<, J=7 Hz) 1.10 (t, 2.1H, $\underline{CH}_3$-CH_2-CH-Br, J=7 Hz) 1.83 (d, 3H, $\underline{CH}_3$-CH-Br, $\underline{CH}_3$-CH-$\overset{+}{N}$<, J=6.5 Hz) 2.00 (m, 2H, -CH_2-)
 $CH_3-\underset{Br}{CH}-\underset{Py^+}{C}(CH_3)_2$	4.9 (1H) q J=7 Hz	-	-	-	1.6 (d, 3H, $\underline{CH}_3$-CH-Br, J=7 Hz) 1.82 (s, 6H, $(CH_3)_2$-C-$\overset{+}{N}$<)
		4.6-5.4 (2H) m	-	-	1.1-2.8 (m, 8H, 4 -CH_2-)
	4.05 (1H) s	5.12 (1H) s			2.05 (m, 5H, 2 -CH_2-, -CH-) 2.77 (m, 1H, -CH-)

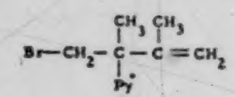
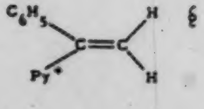
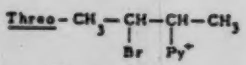
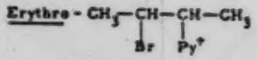
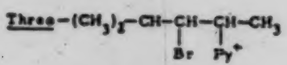
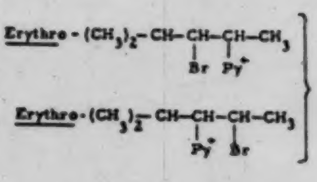
Continued . . .

Table 38 - Continued

Compounds†	δ TMS $(CD_3)_2SO$ $-CH-Br$	$-CH-\overset{+}{N}<$	$-CH_2-Br$	$-CH_2\overset{+}{N}<$	Additional absorptions
 $CH_3-CH_2-O-\underset{Py^+}{\underset{\vert}{CH}}-CH_2-Br$	-	6.57 (1H) t J=5 Hz	4.2 (2H) d J=5 Hz	-	1.23 (t, 3H, $-CH_3$, J=7 Hz) 3.8 (m, 2H, $-CH_2-O-$)
	4.8 (1H) m	6.33 (1H) d J=10 Hz	-	-	3.6-4.5 (m, 2H, $-CH_2-O-$) 1.5-2.5 (m, 4H, 2 $-CH_2-$)
	4.9-5.6 (2H) m		-	-	2.9 (m, 4H, 2 $-CH_2-$) 5.8 (m, 2H, olefinic hydrogens)
	4.7-5.6 (5H) m		-	-	1.6-3.1 (m, 7H, 3 $-CH_2-$, $-CH-$)
 $CH_3-\underset{Br}{\underset{\vert}{CH}}-\underset{Py^+}{\underset{\vert}{CH}}-CH=CH-CH_3$	5.00 (0.58H) m				
 $CH_3-\underset{Py^+}{\underset{\vert}{CH}}-CH=CH-\underset{Py^+}{\underset{\vert}{CH}}-CH_3$ ‡	5.85 (1.42H) m		-	-	1.6-1.9 (m, 6H, 2 $-CH_3$) 6.1-6.55 (m, 2H, olefinic hydrogens)

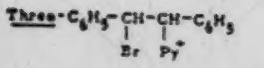
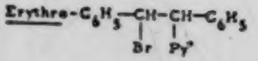
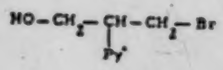
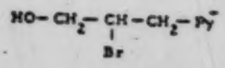
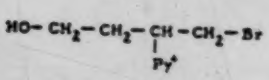
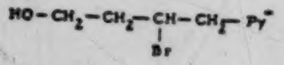
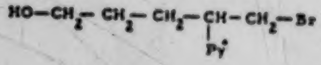
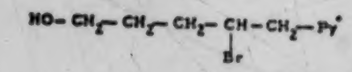
Continued . . .

Table 38 - Continued

Compounds[†]	δ_{TMS} $(CD_3)_2SO$				Additional absorptions
	$-CH-Br$	$-CH-\overset{+}{N}<$	$-CH_2-Br$	$-CH_2-\overset{+}{N}<$	
 $Br-CH_2-\overset{CH_3}{\underset{Py^+}{C}}-\overset{CH_3}{C}=CH_2$	-	-	4.7 (2H) q J=12 Hz	-	1.7 (s, 3H, CH_3-C=C-) 2.13 (s, 3H, CH_3-C-$\overset{+}{N}<$) 5.32 (s, 1H, 1 -CH=) 5.45 (m, 1H, 1 -CH=)
$\overset{+}{Py}-CH_2-C(CH_3)=C(CH_3)-CH_2-\overset{+}{Py}$[*]	-	-	5.4 (4H) s	-	1.8 (s, 6H, 2 -CH_3)
 [§]	-	-	-	-	6.10 (d, 1H, $C_6H_5\diagdown\!=\!\diagdown\underline{H}$, J=2.5 Hz) 6.43 (d, 1H, $C_6H_5\diagdown\!=\!\diagup\underline{H}$, J=2.5 Hz) 7.47 (m, 5H, aromatic hydrogens)
 $\underline{Threo}-CH_3-\underset{Br}{CH}-\underset{Py^+}{CH}-CH_3$	4.7-5.5[*] (2H) m		-	-	1.83 (d, 6H, 2 -CH_3, J=6.5 Hz)
 $\underline{Erythro}-CH_3-\underset{Br}{CH}-\underset{Py^+}{CH}-CH_3$	4.85 (1H) octet J=5, 7 Hz	5.31 (1H) octet J=5, 7 Hz	-	-	1.67 (d, 3H, $\underline{CH}_3$-CH-Br, J=7 Hz) 1.80 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=7 Hz)
 $\underline{Threo}-(CH_3)_2-CH-\underset{Br}{CH}-\underset{Py^+}{CH}-CH_3$	4.6-5.6 (2H) m		-	-	1.33 (2 overlapping doublets, 6H, $(\underline{CH}_3)_2$-CH) 1.80 (d, 3H, $\underline{CH}_3$-CH-$\overset{+}{N}<$, J=6.5 Hz) 2.15 (m, 1H, -$\underline{CH}$ $(CH_3)_2$)
 $\left.\begin{array}{l}\underline{Erythro}-(CH_3)_2-CH-\underset{Br}{CH}-\underset{Py^+}{CH}-CH_3\\ \underline{Erythro}-(CH_3)_2-CH-\underset{Py^+}{CH}-\underset{Br}{CH}-CH_3\end{array}\right\}$	4.2-5.6 (2H) m		-	-	0.7-1.2 (m, 6H, $(\underline{CH}_3)_2$-CH-) 1.6 (m, 1H, -$\underline{CH}$-$(CH_3)_2$) 1.82 (d, 3H, -CH_3)

Continued . . .

Table 38 - Concluded

Compounds[†]	δ_{TMS} $(CD_3)_2SO$ $-CH-Br$	$-CH-\overset{+}{N}<$	$-CH_2-Br$	$-CH_2-\overset{+}{N}<$	Additional absorptions
 **Threo**-$C_6H_5-\underset{Br}{CH}-\underset{Py^+}{CH}-C_6H_5$	7.02 (1H) d J=12 Hz				7.2-7.9 (m, 11H, $-CH-\overset{+}{N}<$, aromatic hydrogens)
 **Erythro**-$C_6H_5-\underset{Br}{CH}-\underset{Py^+}{CH}-C_6H_5$	6.72 (1H) d J=12 Hz	7.18 (1H) d J=12 Hz			7.3-8.2 (m, 12H, aromatic hydrogens, 2 pyridine hydrogens)
 $HO-CH_2-\underset{Py^+}{CH}-CH_2-Br$	4.5-5.5 (3H) m				3.8-4.4 (m, 5H, $-CH_2-Br$, CH_2-OH)
 $HO-CH_2-\underset{Br}{CH}-CH_2-Py^+$					
 $HO-CH_2-CH_2-\underset{Py^+}{CH}-CH_2-Br$	5.25 (1H) m		4.27 (1.7H) t J=6.5, 8 Hz	4.9 (0.3H) m	3.3-3.9 (m, 2H, CH_2-O) 1.3-2.5 (m, 2H, $-CH_2-$)
 $HO-CH_2-CH_2-\underset{Br}{CH}-CH_2-Py^+$					
 $HO-CH_2-CH_2-CH_2-\underset{Py^+}{CH}-CH_2-Br$	5.35 (1H) m		4.35 (1.2H) m	4.9 (0.8H) m	3.4-4.0 (m, 2H, $-\underline{CH_2}-OH$) 1.3-2.5 (m, 4H, 2 $-CH_2-$)
 $HO-CH_2-CH_2-CH_2-\underset{Br}{CH}-CH_2-Py^+$					

[*] All these compounds had absorptions due to Py^+ between δ 8-9.5.

[†] Unless otherwise indicated the counter ion was nitrate

[‡] The counter ions were bromide and nitrate.

[§] The counter ion was bromide.

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